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L4 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:370946 Document No.: PREV200200370946. Antibodies against the stalk
region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis.
Caven, Timothy Hays ; Li, Ma, Chock, Li ; Beavil, Rebecca; Beavil, Andrew;
Ghirlandi, Rodolpho; Gould, Hannah; Conrad, Daniel A. ; Virginia
Commonwealth University, 1517 East Marshall Street, Richmond, VA, 23298
USA. FASEB Journal, March 22, 2002 Vol. 16, No. 6, pp. A1239.
<http://www.fasebj.org/>. print. Meeting Info: Annual Meeting of
Professional Research Scientists on Experimental Biology New Orleans,
Louisiana, USA April 20-24, 2002 ISSN: 0893-0688. Language: English.
AB The stalk region of human CD23 comprising a.a. 41-153 was expressed in E.
coli and purified. In addition a **chimeric human**
CD23 was prepared consisting of the extracellular region of CD23
linked to a modified leucine zipper (LC-CD23). Polyclonal antisera were
produced in rabbits and shown to block binding of IgE to CD23 both on cell
surfaces as well as the interaction of LC-CD23 with IgE in an ELISA based
assay. The antisera was also shown to inhibit IgE synthesis in an
anti-CD14 IL-4 stimulated human PB1 model. The inhibition was dose
dependent and essentially complete blockage of IgE production was seen at
a relatively low dose of anti-stalk. FACS analysis using CD23-B

Lymphoblastoid cells indicated little if any endocytosis and/or protection from cleavage induced by the anti-stalk. Monoclonal antibodies against the human stalk have also been prepared and these are being analysed for the capacity to inhibit IgE binding and IgE synthesis, as well as compare their efficacy to the anti-lectin mabs. The results indicate that targeting the stalk region is efficacious with respect to blocking IgE production.

=> s 12 and CD23 antibody
L5 1 12 AND CD23 ANTIBODY

=> s antibody?
L6 2321935 ANTIBOD?

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L7 3178 16 AND CD23

=> s 17 and humanized
L8 16 17 AND HUMANIZED

=> s 18 and primate
L9 1 18 AND PRIMATE

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L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human
CD23 monoclonal antibodies and use thereof as
therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko
(Idex Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO
9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ,
BA, BE, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH,
GM, GR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RC, RU, SD, SE, SG, SI, SK,
SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA,
GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English).
CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US
1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind human **CD23**
, the low affinity receptor for IgE (FcεRII/CD23), and contain
either a human gamma-1 or human gamma-3 const. domain, are disclosed. The
antibodies are useful for modulating or inhibiting induced IgE
expression. Accordingly, they have practical utility in the treatment or
prophylaxis of disease conditions wherein inhibition of induced IgE prodn.
is therapeutically desirable, including allergic conditions, autoimmune
diseases and inflammatory diseases.

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L10 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human
antibody composition. Hanna, Maril (Idex Pharmaceuticals, USA).
PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W:
AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK,
EE, ES, FI, GB, GE, GM, GR, HU, ID, IL, IN, JP, KE, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,

NZ, PL, PT, RO, RU, RW; AT, BE, BG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MP, NE, NL, PT, SE, SN, TI, TG, TR. English.
 CODEN: EMMXND. APPLICATION: WO 2001-052902 20010919. PRIORITY: US 2000-072571 20001022.

- AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, CD23, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L10 ANSWER 3 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 2001036169 EMBASE Anti-IgE-**antibodies** in the treatment of allergic diseases. Soler M. M. Soler, Pulmonary Division, University Hospital, CH-4031 Basel, Switzerland. msoler@uhbs.ch. Revue Francaise d'Allergologie et d'Immunologie Clinique 42/1 45-49 2002.
 Refs: 25.
 ISSN: 0335-7457. CODEN: RFAIBB. Pub. Country: France. Language: English. Summary Language: English; French.

- AB In an established type-I allergy, the IgE molecule is the main mechanism by which the organism specifically recognizes the inhaled allergen. When the IgE molecule is bound to its high-affinity receptor on the surface of a mast cell, it also provides the link between the allergen and the immediate mast cell activation and mediator release, which are the central steps in the type-I immune response. The **humanized monoclonal Anti-IgE antibody** omalizumab binds to free IgE molecules in the serum and thereby prevents them from attaching to the high affinity IgE-receptors on the mast cell surface. This treatment, when given on a regular basis, is able to block the antigen-induced tissue responses in the bronchi and in the skin. In large scale clinical trials it proved to be effective in controlling allergic asthma, preventing exacerbations and reducing the need for inhaled and/or systemic steroid treatment. In more than 1500 patients treated for at least 1 year, the compound showed excellent safety and tolerability. This new treatment may have an important place in the future treatment of moderate to severe allergic asthma, especially if the patient needs a complex treatment that still allows for recurrent exacerbations. A major advantage of this treatment lies in its ability to control nasal and eye symptoms of the allergic disease at the same time. .COPYRGHT. 2002 Editions scientifiques et medicales Elsevier SAS.

L10 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
 2001:747174 Document No. 135:287537 Inhibitors for the formation of soluble human **CD23** and their use in treatment of diseases. Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20010310, 29 pp.
 DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. English. CODEN: EMMXND.
 APPLICATION: EP 2000-197815 20000405.

- AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is described in which the overprodn. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. **CD23** which inhibitor decreases or blocks selectively the activity of the metalloprotease A1AP which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. **CD23** is a monoclonal or polyclonal **antibody** directed against the metalloprotease A1AP or wherein the inhibitor is an antisense oligonucleotide which is specific for 3'-mmp. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of A1AP as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and allergy.

0001262398 Document Number: E12103341. PubMed ID: 11307028.

Humanized anti-IgE mAb Hu-901 prevents the activation of allergen-specific T cells. van Neerven P J; van Koozen C P; Thomas W P; de Boer M; Knol E F; Davis F M. Tanox Pharma BV, Amsterdam, The Netherlands. joost.vanneerven@tanox.nl. INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, 2001 Jan-Mar; 124 (1-3): 400-2. Journal code: S01652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English. **AB** **BACKGROUND:** As a result of the very efficient capture of allergens by IgE that focuses to **CD23** on B cells or Fc epsilon RI on dendritic cells, allergen-specific T cells can be activated after exposure to very low levels of allergens. This IgE-mediated allergen presentation is 100- to 1,000-fold more efficient than fluid phase endocytosis. The aim of the present study was to determine whether **humanized anti-IgE mAb Hu-901** can prevent the activation of allergen-specific T cells by inhibiting IgE-mediated allergen presentation. **METHODS:** A house dust mite major allergen Der p 1-specific T cell line was generated from an allergic asthma patient, and a model was set up to show IgE-facilitated allergen presentation via **CD23** on EBV-transformed B cells. In addition, experiments were performed by FACS analysis, detecting the presence of IgE-allergen complexes bound to EBV-B cells by polyclonal FITC-labeled anti-IgE antisera. **RESULTS:** The anti-IgE mAb Hu-901 inhibited proliferation of allergen-specific T cells at low allergen concentrations. Inhibition was dose-dependent. This effect could be explained by Hu-901 inhibition of binding of allergen-IgE complexes to **CD23** expressed on EBV-transformed B lymphocytes. **CONCLUSIONS:** These data clearly indicate that anti-IgE **antibodies** for the treatment of allergy exert their effect not only by inhibiting mast cell/basophil degranulation, but also by preventing T cell activation, which possibly explains the effect of anti-IgE treatment on late-phase reactions noted in clinical studies. Copyright 2001 S. Karger AG, Basel

L10 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS

2001:361001 Document No. 136:52380 Allergen, IgE and mast-cell-directed therapies: An overview. Larche, Mark; Kay, A. Barry (Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College School of Medicine, London, UK). Progress in Respiratory Research, 31(New Drugs for Asthma, Allergy and COPD), 182-185 (English) 2001. CODEN: PRRRAE. ISSN: 1422-2140. Publisher: S. Karger AG.

AB A review. In addition to traditional drug development strategies, a no. of current approaches focus on modulation of the immune response to allergens or the allergens themselves. Disease-modulating specific immunotherapy has been used for many years and has been shown to be efficacious, although this form of treatment is slow and carries the risk of systemic adverse reactions. The identification of naturally occurring allergen isoforms of the native protein which do not bind IgE has led to modification of a no. of allergens by site-directed mutagenesis. Such proteins have a reduced or absent interaction with IgE while retaining much of their ability to stimulate T cells. The improved safety profile of such moles. may result in larger, more efficacious doses of protein being given with improved safety. Fragments of allergen moles., such as peptides, are also under development, employing a similar rationale of destroying IgE binding epitopes while retaining T cell determinants. Neutralization of specific moles. in the inflammatory cascade is currently being addressed with "**humanized**" monoclonal **antibodies** and sol. receptors/receptor antagonists, directed towards IgE, cytokines such as IL-4 and IL-5, and cell surface moles. such as **CD23**.

L1 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS

2001:361019 Document No. 134:16590 Treating allergic diseases with immunotherapy and IgE antagonists. Larche, Mark; Van Neerven, Joost; Tanox, Inc., USA. PAT. Int. Appl. No. 99/011796 A1. Pub. No. 99/011796 A1. DESIGNATED STATES: W: AU, AM, AG, AD, BR, BG, BF, BY, CA, CN, CU, CD,

EE, ES, FI, GE, GR, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NC, NZ, PL, RC, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UY, VN, YU, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MP, NE, NL, PT, SE, SN, TD, TG.

English. CODEN: PIXXD2. APPLICATION: WO 99/013446 19990516. PRIORITY: US 1999-PV136168 19990526.

- AB The invention relates to methods of treating allergic diseases with a combination of immunotherapy and IgE antagonists by inhibiting the binding of IgE mols. to IgE receptors. UgrE Fc receptor type 1 and **CD23**, expressed by cells of the immune system. In one embodiment, anti-IgE **antibodies** are used and allergy inhibitors. Disclosed is a mouse (TES-C21) and chimeric mouse-human (TESC-2) anti-IgE **antibody** and fragments as allergy inhibitors.

L10 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS

2000:457197 Document No. 133:57697 Enhanced proteins production in cell culture stimulated by unusually low alkanolic acid concentrations. Islam, Seema; Sharp, Nigel Alan (Glaxo Group Limited, UK). PCT Int. Appl. WO 2000/39282 Al 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GR, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NC, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MP, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP10157 19991221. PRIORITY: GB 1998-28624 19981223.

- AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkanolic acid or its salt at a maintained concn. of less than 0.1mM. Thus, NSO cells transfected with an IgG1 **humanized anti-CD23 antibody** was cultured for 56 days in a draw and fill repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in **antibody** prodn. over the control.

L10 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS

1999:736930 Document No. 131:350265 **Antibodies to CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 99/58679 Al 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GE, GR, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NC, NZ, PL, PT, RC, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UY, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MP, NE, NL, PT, SE, SN, TD, TG. English. CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9639 19980509.

- AB The authors disclose the prepn. and characterization of murine monoclonal and **humanized antibodies** which bind to the **CD23** Fc-epsilonR111 receptor antigen. In one example, **humanized IgG1**, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assoc. rates of the order of $1.5 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L10 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS

1999:64934 Document No. 130:118713 Gamma-1 and gamma-2 anti-human **CD23 monoclonal antibodies** and use thereof as therapeutics. Reiff, Mitchell E.; Kissetter, William S.; Nakamura, Takehiko

Yield Pharmaceuticals Corp., USA; Seikagaku Corp., J. PCT Int. Appl. WO 93/07999 A1 19990827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GR, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NC, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, EE, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English. CODEN: PIXXD2. APPLICATION: WO 1995-US2053 19950217. PRIORITY: US 1997-03085 19970220.

- AB Monoclonal **antibodies** which specifically bind human **CD23**, the low affinity receptor for IgE FcεRII/CD23, and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L10 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380154 Document No. 125:56235 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, EE, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SI, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

- AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD114+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L10 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul Glaxo Group Limited, UK. PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, EE, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SI, TD, TG. English. CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

- AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** **antibody**, **CD23**-liposomes bind to CD114+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of

monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L10 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS
1995:789548 Document No. 123:196599 IgE antagonists for treatment of parasitic infection. Amiri, Payman; Haak-Franscho, Mary; Jardieu, Paula M. Genentech, Inc., USA. FCT Int. Appl. WO 9619181 A1 19960720, 28 pp. DESIGNATED STATES: W: JP, MX; RW: AT, BE, BF, BJ, BR, CH, CL, CM, DE, DK, ES, FR, GB, GR, IE, IT, LU, NL, NO, NZ, PE, SE, SN, TD, TG. English. CITED: PAMCO. APPLICATION: WO 1995-0387 19951105. PRIORITY: US 1994-184083 19940619.

A5 This invention concerns a method for the prevention and treatment of parasitic infection by administering an IgE antagonist. The invention further concerns pharmaceutical compns. and bispecific mols. useful in such method. In example, anti-IgE monoclonal **antibody** reduced serum IgE, serum interleukin 4 and interferon .gamma., number of adult worms and eggs, and hepatosplenomegaly following Schistosoma mansoni infection in mice. The IgE antagonist also reduced the enhancement of **CD23** expression in splenic lymphoid cells.

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L2 150 S L1 AND INHIBIT IGE
L3 0 S L2 AND "ANTI HUMAN CD23"
L4 1 S CHIMERIC HUMAN CD23
L5 0 S L2 AND CD23 ANTIBODY
L6 2321935 S ANTIBODY
L7 3178 S L6 AND CD23
L8 16 S L7 AND HUMANIZED
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L13 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
1995:150073 Document Number: 2019-073. PubMed ID: 10694897. In vitro IgE inhibition in B cells by anti-**CD23** monoclonal **antibodies** is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Plescher W S; Brans R; Hattikatah K; Chamat S; Cao W; Labadie M S; Chinn R C; Morona P A; Shestakow V W S; Li W F; Chen A; Peit M E. Sankyo Corporation, Tokyo Research Institute, Tokyo, Japan. INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 20 Feb 2002, 24:31-41. Journal code: 0273-2378, ISSN: 0273-2378, PUB. country: ENGLAND, United Kingdom. Language: English.

A5 **CD23**, the low affinity receptor for IgE Fc-gamma-receptor II, is

involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23. Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED) monoclonal antibodies. PRIMATIZED p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED p5E8G4, was not as effective in IgE inhibition. An F(ab')₂ of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')₂ of p5E8G1, the F(ab')₂ of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-CD23 antibodies inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

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=> s primatized CD23
L14      0 PRIMATIZED CD23
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=> d his
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(FILE 'HOME' ENTERED AT 13:19:26 ON 05 JUL 2002)
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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 13:19:38 ON 05 JUL 2002
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L1      10122901 S METHOD
L2      150 S L1 AND INHIBIT IGE
L3      0 S L2 AND "ANTI HUMAN CD23"
L4      1 S CHIMERIC HUMAN CD23
L5      0 S L2 AND CD23 ANTIBODY
L6      2321935 S ANTIBODY?
L7      3178 S L6 AND CD23
L8      16 S L7 AND HUMANIZED
L9      1 S L8 AND PRIMATE
L10     12 IUF REMOVE L8 4 DUPLICATES REMOVED
L11     0 S MONKEY ANTI HUMAN CD23
L12     5 S L7 AND HUMAN GAMMA 1 CONSTANT REGION
L13     1 IUF REMOVE L12 4 DUPLICATES REMOVED
L14     0 S PRIMATIZED CD23
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=> s L7 and human IgG1 Fc
L15      3 L7 AND HUMAN IGG1 FC
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=> dup remove L15
PROCESSING COMPLETED FOR L15
L16      1 IUF REMOVE L15 3 DUPLICATES REMOVED
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=> d L16 chim abs
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L16 ANSWER 1 OF 1 MEDLINE 1 DUPLICATE 1
Abstract: Document Number: 947355 L. PubMed ID: 131756. Soluble forms of
CD23 inhibit biologic responses of human B cells. Fanslow W C; Anderson L
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M; Grahstein K H; Clark E A; Cosman D; Armitage R J. Department of Immunology, Immunex Research and Development Corporation, Seattle, WA 98101. JOURNAL OF IMMUNOLOGY, 1992 Jul 15; 149: 2: 658-69. Journal code: 0022-1767. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We have expressed the CD40 surface Ag as both a soluble 23-kDa molecule and a 57-kDa Fc fusion protein containing the **human IgG1 Fc** region. Soluble CD40 and the Fc fusion protein inhibited the proliferative response of anti-IgM-activated human B cells to the CD40 mAb GC8-5. Similarly, GC8-5- and IL-4-induced IgE secretion from PBMC depleted of T cells was effectively blocked by both forms of soluble CD40. Although the soluble constructs of CD40 had only a minimal inhibitory effect on IL-4-mediated proliferation of anti-IgM-activated B cells, IL-4-induced soluble **CD23** shedding from both PBMC and T cells depleted of PBMC, and IgE secretion from PBMC, were significantly reduced in a concentration-dependent manner when soluble CD40 was present in the culture. The data presented demonstrate that both soluble forms of the CD40 molecule are biologically active, and suggest that the ligand for CD40 is inducible in IL-4-stimulated cultures and that it mediates both shedding of sCD23 and IgE secretion.

=> s 17 and humanized

L17 16 L7 AND HUMANIZED

=> dup remove L17

PROCESSING COMPLETED FOR L17

L18 12 DUP REMOVE L17 (4 DUPLICATES REMOVED)

=> d 118 1-12 cbib abs

L18 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS

2002:220424 Document No. 136:246408 Combination therapy for treatment of autoimmune diseases using B cell depleting/immunoregulatory

antibody combination.. Hanna, Nabil (Idex Pharmaceuticals, USA).

PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W:

AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ,

EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KE, KR, LK, LR, MM, MG, MX, NO,

NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA,

GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English).

CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US

2000-PV257147 20001222.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40 **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L18 ANSWER 2 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

2002:36168 EMBASE Anti-IgE-**antibodies** in the treatment of allergic diseases. Soler M. M. Soler, Pulmonary Division, University Hospital, CH-4001 Basel, Switzerland. m.soler@uhbs.ch. Revue Francaise d'Allergologie et d'Immunologie Clinique 42: 1: 48-49 2001.

Refs: 25.

ISSN: 0378-4357. CODEN: RFAIEB. Pub. Country: France. Language: English.

Summary Language: English; French.

AB In an established type-I allergy, the IgE molecule is the main mechanism by which the organism specifically recognizes the inhaled allergen. When the IgE molecule is bound to its high-affinity receptor on the surface of a mast cell, it also provides the link between the allergen and the immediate mast cell activation and mediator release, which are the central steps in the type-I immune response. The **humanized monoclonal**

Anti-IgE **antibody** smallmolecule binds to free IgE molecules in the serum and thereby prevents them from attaching to the high affinity IgE-receptors on the mast cell surface. This treatment, when given on a regular basis, is able to block the antigen-induced tissue responses in the bronchi and in the skin. In large scale clinical trials it proved to be effective in controlling allergic asthma, preventing exacerbations and reducing the need for inhaled and/or systemic steroid treatment. In more than 1000 patients treated for at least 1 year, the compound showed excellent safety and tolerability. This new treatment may have an important place in the future treatment of moderate to severe allergic asthma, especially if the patient needs a complex treatment that still allows for recurrent exacerbations. A major advantage of this treatment lies in its ability to control nasal and eye symptoms of the allergic disease at the same time. .COPYRGHT. 2002 Editions scientifiques et medicales Elsevier SAS.

L18 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS

2001:747174 Document No. 135:287537 Inhibitors for the formation of soluble human **CD23** and their use in treatment of diseases. Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXKXW. APPLICATION: EP 2000-107515 20000407.

AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is described in which the overprodn. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. **CD23** which inhibitor decreases or blocks selectively the activity of the metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. **CD23** is a monoclonal or polyclonal **antibody** directed against the metalloprotease ADAM9 or wherein the inhibitor is an antisense oligonucleotide which is specific for c-myc. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and allergy.

L18 ANSWER 4 OF 12 MEDLINE DUPLICATE 1
2001262398 Document Number: 21203341. PubMed ID: 11307028.

Humanized anti-IgE mAb Hu-901 prevents the activation of allergen-specific T cells. van Neerven R J; van Roomen C P; Thomas W R; de Boer M; Knol E P; Davis F M. (Tanox Pharma BV, Amsterdam, The Netherlands. joost.vanneerven@tanox.nl). INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Jan-Mar) 124 (1-3) 400-2. Journal code: 5211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: As a result of the very efficient capture of allergens by IgE that focuses to **CD23** on B cells or FcεpsilonR1 on dendritic cells, allergen-specific T cells can be activated after exposure to very low levels of allergens. This IgE-mediated allergen presentation is 100- to 1,000-fold more efficient than fluid phase endocytosis. The aim of the present study was to determine whether **humanized anti-IgE mAb Hu-901** can prevent the activation of allergen-specific T cells by inhibiting IgE-mediated allergen presentation. METHODS: A house dust mite major allergen Der p 1-specific T cell line was generated from an allergic asthma patient, and a model was set up to show IgE-facilitated allergen presentation via **CD23** on EBV-transformed B cells. In addition, experiments were performed by FACS analysis, detecting the presence of IgE-allergen complexes bound to EBV-B cells by polyclonal FITC-labeled anti-IgE antisera. RESULTS: The anti-IgE mAb Hu-901 inhibited proliferation of allergen-specific T cells at low allergen concentrations. Inhibition was dose-dependent. This effect could be explained by Hu-901 inhibition of binding of allergen-IgE complexes to **CD23** expressed on EBV-transformed B lymphocytes. CONCLUSIONS: These data

- CH, CI, CK, CL, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SH, TD, TG. (English). CODEN: PIXXLD. APPLICATION: WO 1999-021057 19991211. PRIORITY: GB 1998-08624 19981023.
- AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkaline acid or its salt at a maintained concn. of less than 0.1mM. Thus, NSC cells transfected with an IgG1 **humanized anti-CD23 antibody** was cultured for 56 days in a draw and full repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.05mM butyrate showed a marked increase in **antibody** prodn. over the control.
- L18 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
1999:736930 Document No. 131:350265 **Antibodies to CD23.**
Bonhefroy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9506679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.
- AB The authors disclose the prepn. and characterization of murine monoclonal and **humanized antibodies** which bind to the **CD23** (Fc ϵ RII receptor) antigen. In one example, **humanized IgG1**, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of $1.5-1.85 \times 10^6$ M⁻¹ s⁻¹ and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.
- L18 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human **CD23 monoclonal antibodies** and use thereof as therapeutics. Reiff, Mitchell E.; Klotzner, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837059 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GR, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SH, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US22283 19980017. PRIORITY: US 1997-033085 19970220.
- AB Monoclonal **antibodies** which specifically bind human **CD23**, the low affinity receptor for IgE Fc ϵ RII **CD23**, and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L18 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonhefroy, Jean-Yves Marcel Paul; Leccanet-Renshop, Myrielle (Glaxo Group Limited, UK). PCT Int. Appl. WO 9837040 A1 19980827, 81 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BE, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GR, HU, ID, IL, JP, KE,

KG, KP, KR, KZ, LK, LR, LT, LU, LV, ML, MG, MK, MN, MW, MX, NC, NZ, PL, PT, RC, RU, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4119 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

- AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 kDa protein expressed on endothelial cells or a 115 kDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L18 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NC, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

- AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** **antibody**, **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L18 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS

1995:789548 Document No. 123:196599 IgE antagonists for treatment of parasitic infection. Amiri, Payman; Haak-Fredrich, Mary; Jardieu, Paula M. (Genentech, Inc., USA). PCT Int. Appl. WO 9519181 A1 19950720, 28 pp. DESIGNATED STATES: W: JP, MX; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US87 19950105. PRIORITY: US 1994-184083 19940315.

- AB This invention concerns a method for the prevention and treatment of parasitic infection by administering an IgE antagonist. The invention further concerns pharmaceutical compns. and bispecific mols. useful in such method. In example, anti-IgE monoclonal **antibody** reduced serum IgE, serum interleukin 4 and interferon .gamma., number of adult worms and eggs, and hepatosplenomegaly following Schistosoma mansoni infection in mice. The IgE antagonist also reduced the enhancement of **CD23** expression in splenic lymphoid cells.

=> s anti human C11b
119 : ANTI HUMAN C11b
=> dup remove 119

PROCESSING COMPLETED FOR LIP
L20 5 DUP REMOVE LIP 1 DUPLICATES REMOVED.

W- d 120 1-5 chib abs

L20 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

2000:200935 Document No.: PREVIOUS:200935. Gamma-1 anti-human CD23 monoclonal antibodies. Reff, Mitchell E. 1; Klotzner, William S.; Nakamura, Takeniko. 1. San Diego, CA USA. ASSIGNEE: IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku Corporation, Suita, Osaka, 565-0871, Japan. Patent Info: US 6011117 January 04, 2000. Official Gazette of the United States Patent and Trademark Office Patents, 1 Jan. 4, 2000, Vol. 1230, No. 1, pp. No pagination. e-file. ISSN: 0098-1133. Language: English.

AB Anti-human CD23 monoclonal antibodies containing human gamma 1 constant domains and therapeutic uses are provided. These antibodies inhibit IL-4 induced IgE production by B-cells significantly greater than antibodies containing other constant domains.

L20 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS

1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. Reff, Mitchell R.; Barnett, Richard Spence; McLachlan, Karen Retta (Idex Pharmaceuticals Corporation, USA). U.S. US 5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. AFFILIATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors Molly and vector combinations for use in the subset cloning method are also provided. This Molly vector contains dihydrofolatereductase, NI-Neomycin phosphotransferase exon1, NI-Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human CD23 antibody and immunoadhesin in Desmond marked CHO cells was achieved.

L20 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS

1999:779157 Document No. 132:19632 Gamma-1 and gamma-3 anti-human CD23 monoclonal antibodies and use thereof as therapeutics. Reff, Mitchell E.; Klotzner, William S.; Nakamura, Takeniko. 1. Idec Pharmaceuticals Corp., USA; Seikagaku Corp., JPT Int. Appl. WO

9837099 AI 19980817, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KH, KP, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MH, MN, MW, MX, NC, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, PU, TJ, TM, RW: AT, BE, BF, BG, BF, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MD, ML, MR, NE, NL, PT, SE, SN, TL, TG. English. CCDEM: BIXMDE. APPLICATION: WO 1998-USL253 19980217. PRIORITY: US 1997-503095 19970222.

- AB Monoclonal antibodies which specifically bind human CD23, the low affinity receptor for IgE FcεRII/CD23, and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The antibodies are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L20 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

1996:463188 Document No.: PREV199699185544. Mechanism of T cell subsets and cytokines in the regulation of IgE production in exogenous asthma. Wang Danqi, Xia Guoguang (1); Zhao Shulin; et al.. (1) Dep. Respiratory Med., Beijing Ji Shui Tan Hosp., Beijing 100035 China. Zhonghua Weishengwuxue He Mianyixue Zazhi, (1996) Vol. 16, No. 4, pp. 299-301. ISSN: 0254-5101. Language: Chinese. Summary Language: Chinese; English.

- AB The peripheral blood of 30 cases of asthma and 30 control adults were measured for T cell subsets with indirect Immunofluorescence of monoclonal antibodies, for IgE, IL-4 with ELISA, for IL-2 with F12-cell line-biological method, for IL-6 with IL-6-dependent cell line 7TD1 intake method and for CD23 with anti human CD23 McAb. The mechanism of T cells and cytokines in the regulation of IgE production in asthma and the effect of cytokines on the pathogenesis of asthma were also studied. The results showed that the levels of IgE, IL-4, IL-2, CD23, CD8+ as well as the ratio of CD4/CD8+ in cases of their acute stage were significantly different from those in their remission stage and normal controls (P lt 0.01). In their remission stage, there was no significant IgE difference between cases and control (P gt 0.05). And there were significant differences of CD8+ CD4/CD8 ratio between cases and normal controls (P lt 0.01). There was no significant difference of CD3, CD4, IL-6 among three groups (P gt 0.05). It indicated that the increased production of IgE antibody was the key factor in the pathogenesis of exogenous asthma and the cytokines played roles in the process of inflammatory reactions in the airway.

L20 ANSWER 5 OF 5 MEDLINE

DUPLICATE 1

91010930 Document Number: 91010930. PubMed ID: 1699879. A bioassay for the measurement of human Interleukin-4. Siegel J F; Mostowski H S. Division of Cytokine Biology, Center for Biologics Evaluation and Research, FDA, Bethesda, MD. JOURNAL OF IMMUNOLOGICAL METHODS, 1999 Sep 14 132 3: 297-35. Journal code: 1365544. ISSN: 0165-1759. Pub. country: Netherlands. Language: English.

- AB We have developed a bioassay for human IL-4 based upon its ability to upregulate CD23 low affinity IgE receptor expression. Ramos, a B lymphocyte line derived from a Burkitt lymphoma, was repetitively subcloned yielding a clone, Ramos.20.210, which is several fold more sensitive to this effect of IL-4. In microtiter plates cells were cultured for 48 h in the presence of dilutions of recombinant human IL-4 or samples, and then stained with routine anti-human CD23 and goat anti-mouse IgG-FITC. IL-4 induced an eight-fold increase in channel shift in fluorescence intensity as measured by flow cytometry. Significant effects were observed at an IL-4 concentration of 5-10³ pg/ml and increased with concentrations up to 10⁴ pg/ml. Inter- and intra-assay coefficients of variation were 10% and 11% respectively. The

bioassay showed good specificity for IL-4; however, tumor necrosis factors alpha and beta, at optimal concentrations, gave readings barely at the threshold of detection.

=> s rempel f?/au or brooks k?/au
L21 1255 PEMPEL F?/AU OR BROOKS K?/AU

=> s L21 and anti CD23
L22 1 L21 AND ANTI CD23

=> s L21 and antibody
L23 83 L21 AND ANTIBODY

=> s L23 and CD23
L24 0 L23 AND CD23

=> s L23 and IgE
L25 1 L23 AND IGE

=> d L25 cblb abs

L25 ANSWER 1 OF 1 MEDLINE
95048595 Document Number: 95048595. PubMed ID: 7525472. B-1 cells in systemic autoimmune responses: IgM⁺, Fc epsilon R^{hi} B cells are lost during chronic graft-versus-host disease but not in murine AIDS or collagen-induced arthritis. Iciek L A; Waldschmidt T J; Griffiths M M; **Brooks K H.** (Department of Microbiology, Michigan State University, East Lansing 48824.) IMMUNOLOGICAL INVESTIGATIONS, (1994 Aug) 23 (4-5) 293-311. Journal code: 8504629. ISSN: 0882-0139. Pub. country: United States. Language: English.

AB The potential role of B-1 cells (i.e. the CD5⁺ B cell and "sister" B cell subsets) in autoimmunity is controversial. CD5⁺ B cells have been shown to secrete **antibodies** of similar specificity as those found in many systemic autoimmune diseases; in addition, increases in CD5⁺ B cell frequency have been reported in patients suffering from rheumatoid arthritis, Sjogren's syndrome, myasthenia gravis, insulin-dependent diabetes mellitus and Hashimoto's thyroiditis. Whether these increases are due to expansion of B-1 lineage cells in the human or due to activation-induced expression of CD5 by conventional B cells is unclear. In the present study, we used three murine models of systemic autoimmunity: murine acquired immunodeficiency syndrome (MAIDS), chronic graft-versus-host disease (cGVHD), and collagen-induced arthritis (CIA) to determine whether increases in B-1 cell frequency are universally seen in models of autoimmunity which are mechanistically distinct. In contrast to the aforementioned human systemic autoimmune diseases which exhibit an increase in CD5⁺ B cell frequency, the percentage of CD5⁺ B cells declined in all three murine models of systemic autoimmune disease. Even though there was a decrease in the frequency of CD5⁺ B cells there was no change in the actual number of CD5⁺ B cells. Thus, the apparent decline in CD5⁺ B cell frequency was due to increases in either T cells, conventional Fc epsilon R⁺ B cells, or both. The only actual decline in a B cell subset was the loss of IgM⁺, Fc epsilon R^{hi} B cells in both the spleen and peritoneal cavity of mice undergoing a chronic graft-versus-host reaction. Therefore, our data suggests that expansion of the B-1 subset does not occur as a general feature of murine systemic autoimmune disease. These observations, consistent with previous studies of Ig gene usage in autoreactive **antibodies**, support the view that expansion and differentiation of the CD5⁺ B cell subset is not a central event leading to autoantibody production.

=> dup remove L25

PROCESSING COMPLETED FOR L23
L26 37 DUP REMOVE L23 46 DUPLICATES REMOVED

=> d 126 1-37 cbib abs

L26 ANSWER 1 OF 37 MEDLINE DUPLICATE 1
2002200719 Document Number: 21904109. PubMed ID: 11906504. Increased expression of the neuronal glutamate transporter EAAT3/EAAC1 in hippocampal and neocortical epilepsy. Orino Peter B; Jin Hong; Skumate Melissa D; Robinson Michael B; Coulter Douglas A; Brooks-Kayal Amy R. PENN Epilepsy Center, Department of Neurology, University of Pennsylvania, Philadelphia, Pennsylvania, USA. J EPILEPSIA, (2002 Mar); 43 (3): 211-8. Journal code: 2983306R. ISSN: 0013-9580. Pub. country: United States. Language: English.

AB PURPOSE: To define the changes in gene and protein expression of the neuronal glutamate transporter (EAAT3/EAAC1) in a rat model of temporal lobe epilepsy as well as in human hippocampal and neocortical epilepsy. METHODS: The expression of EAAT3/EAAC1 mRNA was measured by reverse Northern blotting in single dissociated hippocampal dentate granule cells from rats with pilocarpine-induced temporal lobe epilepsy (TLE) and age-matched controls, in dentate granule cells from hippocampal surgical specimens from patients with TLE, and in dysplastic neurons microdissected from human focal cortical dysplasia specimens. Immunolabeling of rat and human hippocampi and cortical dysplasia tissue with EAAT3/EAAC1 antibodies served to corroborate the mRNA expression analysis. RESULTS: The expression of EAAT3/EAAC1 mRNA was increased by nearly threefold in dentate granule cells from rats with spontaneous seizures compared with dentate granule cells from control rats. EAAT3/EAAC1 mRNA levels also were high in human dentate granule cells from patients with TLE and were significantly elevated in dysplastic neurons in cortical dysplasia compared with non-dysplastic neurons from postmortem control tissue. No difference in expression of another glutamate transporter, EAAT2/GLT-1, was observed. Immunolabeling demonstrated that EAAT3/EAAC1 protein expression was enhanced in dentate granule cells from both rats and humans with TLE as well as in dysplastic neurons from human cortical dysplasia tissue. CONCLUSIONS: Elevations of EAAT3/EAAC1 mRNA and protein levels are present in neurons from hippocampus and neocortex in both rats and humans with epilepsy. Upregulation of EAAT3/EAAC1 in hippocampal and neocortical epilepsy may be an important modulator of extracellular glutamate concentrations and may occur as a response to recurrent seizures in these cell types.

L26 ANSWER 2 OF 37 MEDLINE DUPLICATE 2
2001183114 Document Number: 21126425. PubMed ID: 11233905. Improved flow cytometric detection of HLA alloantibodies using pronase: potential implications in renal transplantation. Vaidya S; Cooper T V; Avandalehi J; Barnes T; Brooks K; Hymel P; Noss M; Sellers P; Thomas A; Stewart D; Taiter J; Fish J C; Gugliuzza K R; Bray R A. Department of Pathology, University of Texas Medical Branch, Galveston 77555-0178, USA. TRANSPLANTATION, (2001 Feb 15); 71 (3): 422-9. Journal code: 01431441. ISSN: 0041-1337. Pub. country: United States. Language: English.

AB BACKGROUND: Flow cytometric crossmatch FCXM has grown in popularity and has become the "standard of practice" in many programs. Although FCXM is the most sensitive method for detecting alloantibody, the B cell FCXM has been problematic. Difficulties with the B cell FCXMs have been centered around high nonspecific fluorescence background owing to Fc-receptors present on the B cells and autoantibodies. To improve the specificity and sensitivity of the B cell FCXM, we utilized the proteolytic enzyme pronase to remove Fc receptors from lymphocytes before their use in FCXM. METHODS: Lymphocytes isolated from peripheral blood, spleen, or lymph nodes were treated with pronase and then used in a three-color FCXM. A total of 147 T- and B cell FCXMs using pronase-treated and untreated cells were performed. Testing used serial dilutions of HLA class II class I and II

class II, with the titer of each **antibody** at one dilution past the titer at which the complement-mediated cytotoxicity anti-human globulin crossmatch became negative. RESULTS: After pronase treatment, the actual channel values of the negative control in both T cell and B cell FCXMs declined from 75+/-11 to 57+/-4 $P<0.05$, and 107+/-11 to 45+/-3 $P<0.0001$, respectively. Pronase treatment resulted in improved sensitivity of the T and B cell FCXM in detecting class I **antibody** by 20% and 60%, respectively. In no instance was a false-positive reaction observed. In this study, pronase treatment improved the specificity of B cell FCXM for detecting class II **antibodies** from 75% to 100% $P=0.02$. In no instance was a false-negative reaction recorded. Lastly, on the basis of these observations we re-evaluated three primary transplant recipients who lost their allografts because of accelerated rejection. One of the patients was transplanted across negative T and B cell FCXM, whereas the other two patients were transplanted across a positive T cell, but negative B cell, FCXM. After pronase treatment, T and B cell FCXMs of each patient became strongly positive, and donor-specific anti-HLA class I **antibody** was identified in each case. CONCLUSION: Utilization of pronase-treated lymphocytes improves both the sensitivity and specificity of the FCXM.

L26 ANSWER 3 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:495043 Document No.: PREV200000495164. Influenza vaccine may induce auto-reactive IgG **antibodies** detectable in flow cytometry crossmatches. Cooper, T. Y. (1); Avandsalehi, J. (1); Hymel, P. (1); Barnes, T. (1); Thomas, A. (1); Sellers, R. (1); Brooks, K. (1); Noor, M. (1); Qiu, S. M. (1); Gugliuzza, K. (1); Daller, J. (1); Vaidya, S. (1). (1) Departments of Pathology and Surgery, University of Texas Medical Branch, Galveston, TX USA. Human Immunology, (2000) Vol. 61, No. Supplement 2, pp. S80. print. Meeting Info.: 26th Annual Meeting of the American Society for Histocompatibility and Immunogenetics Lake Buena Vista, Florida, USA October 10-14, 2000 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English. Summary Language: English.

L26 ANSWER 4 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1999:472830 Document No.: PREV199900472830. High background fluorescence may contribute to false negative B lymphocyte flow cytometry crossmatches. Cooper, T. (1); Hymel, P. (1); Thomas, A. (1); Brooks, K. (1); Avandsalehi, J. (1); Stewart, D.; Bray, R.; Vaidya, S. (1). (1) Department of Pathology, The University of Texas Medical Branch, Galveston, TX USA. Human Immunology, (1999) Vol. 60, No. SUPPL. 2, pp. S140. Meeting Info.: 25th Annual Meeting of the American Society for Histocompatibility and Immunogenetics New Orleans, Louisiana, USA October 20-24, 1999 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 5 OF 37 SCISEARCH COPYRIGHT 2002 ISI R.
1998:483339 The Genuine Article R Number: 2084C. Modulation of IL-1 beta, IL-6 and TNF-alpha secretion and mRNA expression by the trichothecene vomitoxin in the RAW 264.7 murine macrophage cell line. Wong S S; Zhou H P; MarinMartinez M L; Brooks K; Festka J C. Reprint. MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, 234 SW TRAUT BLDG, E LANSING, MI 48824 Reprint; MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, E LANSING, MI 48824; MICHIGAN STATE UNIV, DEPT ENVIRONMENTAL TOXICOLOGY, E LANSING, MI 48824; MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, NATL CTR FOOD SAFETY & TOXICOL, E LANSING, MI 48824. FOOD AND CHEMICAL TOXICOLOGY MAY 1998 Vol. 36, No. 5, pp. 479-489. Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, WILLINGTON, OXFORD OX6 4BS, ENGLAND. ISSN: 0273-2312. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AMI FULL FORMATS

AB Oral exposure of mice to vomitoxin (V) has been previously shown to

enhance gene expression of several cytokines associated with macrophage activation. Here, the effects of exposure to VT in vitro on cytokine secretion and mRNA expression were determined in the murine macrophage cell line RAW 264.7. Enzyme-linked immunosorbent assay (ELISA) of supernatants revealed that significant increases in secreted tumour necrosis factor alpha (TNF-alpha) were observed 2 days after exposure to VT at 100 ng/ml and 250 ng/ml, both with and without lipopolysaccharide (LPS) activation. While VT did not affect IL-6 secretion in the absence of LPS, significantly increased IL-6 production was observed in culture supernatants after 1, 3 and 5 days of exposure to VT at 250 ng/ml in the presence of LPS. Soluble IL-1 beta was not detected in control or VT-treated cell cultures with or without LPS activation. Immunohistochemical staining of intracellular cytokines in conjunction with flow cytometric analysis was used to detect the effects of VT on the percentage of positive cells and output per cell. The percentage of cells that produced intracellular TNF-alpha were significantly increased at 100 and 250 ng/ml VT with and without LPS whereas increased IL-6 output per cell was observed at 100 and 250 ng/ml VT with LPS. To assess the effects of VT on cytokine mRNA expression, RAW 264.7 cells were analysed semi-quantitatively using reverse transcription-polymerase chain reaction (RT-PCR) in conjunction with Southern hybridization analysis. Elevated TNF-alpha mRNA was observed at 100 and 250 ng VT/ml at 6 and 24 hr in the absence of LPS. With the addition of LPS, superinduction of TNF-alpha was not observed in the presence of VT. Increased IL-1 beta and IL-6 mRNAs were observed at 100 and 250 ng VT/ml at 24 hr in the presence of LPS. These results demonstrated that VT could superinduce both cytokine secretion and mRNA levels in macrophage cultures. (C) 1998 Elsevier Science Ltd. All rights reserved.

L26 ANSWER 6 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)

1999:182785 The Genuine Article (R) Number: YZ186. Role of macrophages in elevated IgA and IL-6 production by Peyer's patch cultures following acute oral vomitoxin exposure. Yan D (Reprint); Zhou H R; Brooks K H; Pestka J J. MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, E LANSING, MI 48824 (Reprint); MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, INST ENVIRONM TOXICOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, NATL FOOD SAFETY & TOXICOL, E LANSING, MI 48824. TOXICOLOGY AND APPLIED PHARMACOLOGY (FEB 1998) Vol. 148, No. 2, pp. 261-273. Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS. 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495. ISSN: 0041-008X. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Oral vomitoxin (VT) exposure in mice results in elevated cytokine gene expression, increased production of IgA, and IgA nephropathy. To determine the potential role of macrophages (M phi) in these effects, an ex vivo model was devised whereby Peyer's patch (PP) and spleen cells were prepared from mice 2 h after oral exposure to 0 or 25 mg/kg body wt VT, cultured, and then evaluated for IgA and cytokine IL-6 production. Both PP and, to a lesser extent, spleen cells from treatment mice produced more IgA over a 7-day period than did corresponding control cells when cultured without a costimulus or in the presence of either phorbol myristate acetate plus ionomycin (PMA + ION) or lipopolysaccharide (LPS); IgA elevation was most marked in LPS-treated cultures. The VT effect was completely ablated in PP cultures that were depleted of M phi but not in M phi-depleted spleen cultures. VT exposure similarly increased production of IL-6, an important helper factor for IgA secretion, in LPS-stimulated PP and spleen cell cultures. IL-6 production was also ablated by M phi depletion. A potential costimulatory role for M phi was further suggested because both IgA and IL-6 production increased when M phi-depleted PP cells from VT-treated animals were recultured with peritoneal M phi from VT-treated animals. Similar effects were observed when an analogous ex vivo approach was used with purified PP B cells and peritoneal M phi. B cells from control animals also secreted elevated levels of IgA when

recultured with splenic CD4⁺ cells from VT-treated animals, thus confirming previous studies showing that T cell help also contributes to increased IgA production. Potential roles for soluble mediators and cell contact in this process were suggested when IgA production was measured in cultures of B6 cells separated from VT-treated M phi by a semipermeable membrane. Taken together, these and previous results suggest that M phi may play a key mechanistic role in elevated IgA production and IgA nephropathy in VT-exposed mice. © 1999 Academic Press.

L26 ANSWER 7 OF 37 MEDLINE DUPLICATE 3
1999:430619 Document Number: 99430619. PubMed ID: 9761452. The glutamate transporter, GLT-1, is expressed in cultured hippocampal neurons.
Brooks-Kayal A R; Munir M; Jin H; Robinson M B. (Department of Neurology, Children's Hospital of Philadelphia, Children's Seashore House, University of Pennsylvania, 19104, USA. Kayal@email.chop.edu).
NEUROCHEMISTRY INTERNATIONAL, (1998 Aug) 33 (2) 95-100. Journal code: 8006955. ISSN: 0197-0186. Pub. country: ENGLAND: United Kingdom. Language: English.

AB There are multiple subtypes of Na⁺-dependent glutamate transporters. Several studies suggest that EAAC1 and EAAT4 are expressed in neurons, while GLT-1 and GLAST expression is thought to be restricted to glia. In the present study, expression of GLT-1 and EAAC1 was examined in cultured rat hippocampal neurons using single cell mRNA amplification and immunocytochemistry with subtype specific antibodies. GLT-1 and EAAC1 mRNAs were observed in all neurons examined. Neuronal phenotype was confirmed in these cells by expression of neurofilament (NF-L) mRNA and absence of glial fibrillary acidic protein (GFAP) mRNA. EAAC1 immunoreactivity was observed in essentially all cells which expressed neuron specific enolase (NSE) and GLT-1 immunoreactivity was detected in the majority (approximately 90%) of NSE-positive cells. Consistent with the glial expression of GLT-1, GLT-1 immunoreactivity was also observed in NSE-negative cells. These studies provide evidence that GLT-1 expression is not intrinsically restricted to glial cells, but can occur in neurons under certain circumstances.

L26 ANSWER 8 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1999:470990 Document No.: PREV199800470990. Impact of positive flow crossmatches on primary renal transplants. Cooper, Todd; Vaidya, Smita; Asfour, M. Ayman; Avandsalehi, Jeanne; Barnes, Titus; **Brooks, Karl**; Lopez, Sheila; Partlow, David; Sellers, Racheal; Thomas, Alice. Univ. Tex. Med. Branch, Galveston, TX USA. Human Immunology, (1998) Vol. 55, No. SUPPL. 1, pp. 7. Meeting Info.: 24th Annual Meeting of the American Society for Histocompatibility and Immunogenetics Vancouver, British Columbia, Canada October 10-15, 1998 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 9 OF 37 MEDLINE DUPLICATE 4
97418734 Document Number: 97418734. PubMed ID: 9274810. Potential role for IL-5 and IL-6 in enhanced IgA secretion by Feyer's patch cells isolated from mice acutely exposed to vomitoxin. Yan D; Zhou H R; **Brooks K H;** Pestka J J. Department of Food Science and Human Nutrition, Michigan State University, East Lansing 48824, USA.
TOXICOLOGY, 1997 Sep 24; 133 (1-2): 145-159. Journal code: 1361755. ISSN: 1303-493X. Pub. country: Ireland. Language: English.

AB Dietary exposure to vomitoxin (VT) results in hyperelevated serum IgA and IgA nephropathy in mice. To assess the possible role of cytokines in this IgA dysregulation, the effects of a single oral exposure in B6JF1 male mice to 1, 5 or 15 mg/kg BW VT on production of IgA and cytokines in Feyer's patch PF and spleen cell cultures were evaluated. IgA levels were increased significantly in PF cell cultures prepared from mice at 1 or 15 mg/kg BW after oral exposure to VT and subsequently stimulated with phorbol myristate acetate (PMA) and ionomycin (ION) or with lipopolysaccharide (LPS). Significant effects on IgA production were not observed in spleen

cell cultures. Since cytokines such as IL-2, IL-4, IL-5 and IL-6 have been shown to promote IgA production, the effect of the same VT exposure regimen on secretion of these mediators was determined in PP and spleen cultures. Supernatant IL-2 and IL-4 levels were unaffected by the prior treatment of animals with VT. In contrast, IL-5 levels were increased significantly in 7-day PP cell cultures obtained 2 h after VT exposure both with and without PMA + ION exposure but not in other cultures. IL-6 levels were increased significantly in LPS-treated cultures prepared from PP at 2 and 24 h following exposure to VT. IL-6 levels were also elevated significantly in both PMA + ION or LPS treated cultures from spleen isolated at 2 h but not 24 h post VT exposure. To determine whether IL-5 or IL-6 play a role in IgA hypersecretion in vitro, PP and spleen cells from mice obtained 2 h after exposure to 25 mg/kg VT were cultured in the presence of neutralizing cytokine antibodies (Abs) and IgA production was monitored. Consistent with IL-5's previously documented role in IgA production, anti-IL-5 decreased IgA levels to background in cultures of both control and VT-exposed PP or spleen cells in the presence of either PMA + ION or LPS. Similar results were seen with addition of anti-IL-6. IgA levels were decreased to a lesser extent in PP cells cultured with LPS and in spleen cells cultured with PMA + ION from VT-exposed mice to which anti-IL-2 Ab was added. Thus, the potential for enhanced IgA production exists in lymphocytes as early as 2 h and as late as 24 h after a single oral exposure to VT and this may be related to the increased capacity to secrete helper cytokines of T cell and macrophage origin. Taken together, the results suggest that the superinduction of cytokine expression may, in part, be responsible for upregulation of IgA secretion in mice exposed orally to VT.

L26 ANSWER 10 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:62941 Document No.: PREV199800062941. Acute rejection of a living related kidney associated with positive T-cell flow cytometry crossmatch. Cooper, T. Y.; Sellers, R. B.; Asfour, M. A.; Lopez, S. B.; Moller-Nichols, M.; Barnes, T. H.; Brooks, K.; Partlow, D.; Avandalehi, J.; Thomas, A.; Vaidya, S. Dep. Pathol., Univ. Texas Med. Branch, Galveston, TX USA. Human Immunology, (1997) Vol. 55, No. SUPPL. 1, pp. 75. Meeting Info.: 23rd Annual Meeting of the American Society for Histocompatibility and Immunogenetics Atlanta, Georgia, USA October 14-19, 1997 The American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 11 OF 37 MEDLINE DUPLICATE 5
96022850 Document Number: 96022850. PubMed ID: 7549055. Clinical importance of pre-mortem blood lymphocytes in cadaver donor tissue typing. Vaidya S; Orchard P; Schroeder W; Haneke R; Brooks K; Thomas A; Corba A; Asfour A; Fish J C. Department of Pathology, University of Texas Medical Branch, Galveston 77555-0546, U.S.A. CLINICAL TRANSPLANTATION, 1999 Jun; 9:3 Pt 1:165-70. Journal code: 8710240. ISSN: 0902-0063. Pub. country: Denmark. Language: English.

AB We have refined our immunomagnetic bead IM bead procedures to isolate pure and viable lymphocyte subpopulation from pre-mortem PM blood for cadaver donor HLA typing, preliminary and final crossmatches. XMs. The results of 1200 XMs were compared using T/B lymphocytes isolated either from PM blood or spleen/lymphnode (SPLN) tissue. IM bead technique was used to isolate T/B cells from PM blood and nylon wool column (NWC) technique was used to isolate T/B cells from SPLN. When we compared the outcome of 80 T-cell crossmatches using T cells from PM blood or SPLN of 8 separate cadaver donors, NWC TXMs tended to be more false-negative for high PFA > 1, total 30 XMs as well as low PFA < 1, total 30 XMs did not reach statistical significance. In contrast, NWC BXM 42 B XM were found to be far more false-negative than IM bead BXM regardless of the PFA of the patients. In order to ensure that NWC BXM were indeed false-negative, 23 sera with known anti-IF antibodies were BXMed where antigen-specific B cells were isolated by both the techniques. Our

results showed that IM bead BXM identified the LR specificities greater than 90% of the time, the titers of ab specificities were stronger 1:8. In comparison, NWB cell XMs were weak titers 1:2, and the false negative rate for some ab was as high as 73%. Using IM bead and NWC techniques we compared our turnaround time (TAT) for cadaver donor typing, preliminary and final XMs. ABSTRACT TRUNCATED AT 250 WORDS.

L26 ANSWER 12 OF 37 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V. DUPLICATE 6
P4251909 EMBASE Document No.: 1994251909. In vitro effects of vomitoxin deoxynivalenol on T-cell interleukin production and IgA secretion. Warner R.L.; Brooks K.; Pestka J.J. Dept. of Food Sci./Human Nutrition, 234 G.M. Trout Bldg., Michigan State University, East Lansing, MI 48824-1224, United States. Food and Chemical Toxicology 32/7 (617-625), 1994.

ISSN: 0278-6915. CODEN: FCTOD7. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The exposure of lymphocyte cultures to vomitoxin was used to determine possible mechanism by which this naturally occurring toxin induces serum immunoglobulin A (IgA) elevation and IgA nephropathy in the mouse. Vomitoxin exposure within the range of 10 to 1000 ng/ml inhibited DNA synthesis, protein synthesis as well as IgA, IgG and IgM production in lymphocyte cultures prepared from the Peyer's patch (PP) and spleen. When purified B cells were cultured in the presence of vomitoxin, inhibition of IgA, IgG and IgM production was similarly observed. However, on 24-hr pulsed co-exposure to vomitoxin and the mitogen concanavalin A (ConA), CD4+/CD8+ cells were capable of inducing a three- to five-fold increase in production of IgA, but not IgG and IgM by cocultured B cells when compared with B cells cocultured with control T cells exposed to the mitogen only. When pulsed for 48 hr with ConA and toxin, CD4+ cells were similarly capable of causing a significant increase in IgA production by B cells. 48-hr pulsed exposure of CD4+ cells to ConA and vomitoxin resulted in significantly increased production of the T helper cytokines IL-4, IL-5 and IL-6 after 5 additional days of culture, compared with ConA-stimulated CD4+ cells alone. These results suggest that vomitoxin was capable of enhancing CD4+-mediated help for IgA production by B cells and that this could possibly be mediated by way of increased cytokine production.

L26 ANSWER 13 OF 37 MEDLINE DUPLICATE 7
P4266212 Document Number: 94266212. PubMed ID: 8206429. Polyspecific and autoreactive IgA secreted by hybridomas derived from Peyer's patches of vomitoxin-fed mice: characterization and possible pathogenic role in IgA nephropathy. Rasooly L; Abouzi M M; Brooks K H; Pestka J J. (Department of Microbiology and Public Health, Michigan State University, East Lansing 48824.) FOOD AND CHEMICAL TOXICOLOGY, (1994 Apr. 32 (4) 337-48. Journal code: 0274483. ISSN: 0278-6915. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A total of 122 immunoglobulin Ig A-producing hybridoma clones were isolated from the Peyer's patches of vomitoxin-fed BALB/c mice and the resultant antibodies were characterized for their antigenic specificity and pathogenic potential. When reactivity was tested against a panel consisting of DNA, sphingomyelin, thyroglobulin, collagen, casein, cardiolipin and bovine serum albumin conjugates of phosphorylcholine, inulin and trinitrophenyl that were representative of self and non-self antigens, approximately 95% of the monoclonal IgAs bound to at least one of the panel antigens and 10% bound to more than one antigen. The polyspecificity of some of the monoclonal IgAs was further suggested by demonstrating the capacity of one antigen to inhibit binding of monoclonal IgA to another antigen. Protein staining and Western blotting of irradiated native polyacrylamide gels, indicated that trimeric IgA predominated in the isolated monoclonal IgAs. Repeated injections of mice with representative monoclonal IgAs induced glomerulonephritis in three of four of the clones tested but not IgA deposition in the kidney glomerulus. In addition, three of the four monoclonal IgAs caused IgG and C3 deposition

in the kidney mesangium. These and previous results suggest that dietary vomitoxin promotes the polyclonal activation and expansion of IgA-secreting B cells at the Peyer's patch level and that resultant polyspecific, autoreactive IgA may contribute to kidney pathogenesis.

L26 ANSWER 14 OF 37 SCISEARCH COPYRIGHT 2002 ISI R
94:364738 The Genuine Article R Number: HQ429. POLYSPECIFIC AND
AUTOREACTIVE IGA SECRETED BY HYBRIDOMAS DERIVED FROM PEYERS-PATCHES OF
VOMITOXIN-FED MICE - CHARACTERIZATION AND POSSIBLE PATHOGENIC ROLE IN IGA
NEPHROPATHY. RASOGLY L; ABCUZIED M M; BROOKS K H; FESTA J C
Reprint: MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, 234 GM TRCUT
BLDG, E LANSING, MI, 48824 Reprint; MICHIGAN STATE UNIV, DEPT FOOD SCI &
HUMAN NUTR, E LANSING, MI, 48824; MICHIGAN STATE UNIV, DEPT MICROBIOL &
PUBL HLTH, E LANSING, MI, 48824. FOOD AND CHEMICAL TOXICOLOGY (APR 1994)
Vol. 32, No. 4, pp. 337. ISSN: 0278-6915. Pub. country: USA. Language:
ENGLISH.

AB *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
A total of 122 immunoglobulin (Ig)A-producing hybridoma clones were
isolated from the Peyer's patches of vomitoxin-fed BALB/c mice and the
resultant **antibodies** were characterized for their antigenic
specificity and pathogenic potential. When reactivity was tested against a
panel consisting of DNA, sphingomyelin, thyroglobulin, collagen, casein,
cardiolipin and bovine serum albumin conjugates of phosphorylcholine,
inulin and trinitrophenol that were representative of self and non-self
antigens, approximately 95% of the monoclonal IgAs bound to at least one
of the panel antigens and 80% bound to more than one antigen. The
polyspecificity of some of the monoclonal IgAs was further suggested by
demonstrating the capacity of one antigen to inhibit binding of monoclonal
IgA to another antigen. Protein staining and Western blotting of gradient
native polyacrylamide gels, indicated that trimeric IgA predominated in
the isolated monoclonal IgAs. Repeated injections of mice with
representative monoclonal IgAs induced microhaematuria in three of four of
the clones tested but not IgA deposition in the kidney glomerulus. In
addition, three of the four monoclonal IgAs caused IgG and C3 deposition
in the kidney mesangium. These and previous results suggest that dietary
vomitoxin promotes the polyclonal activation and expansion of
IgA-secreting B cells at the Peyer's patch level and that resultant
polyspecific, autoreactive IgA may contribute to kidney pathogenesis.

L26 ANSWER 15 OF 37 MEDLINE DUPLICATE 8
95048595 Document Number: 95048595. PubMed ID: 7525472. B-1 cells in
systemic autoimmune responses: IgM+, Fc epsilon Rdu11 B cells are lost
during chronic graft-versus-host disease but not in murine AIDS or
collagen-induced arthritis. Iciek L A; Waldschmidt T J; Griffiths M M;
Brooks K H. (Department of Microbiology, Michigan State
University, East Lansing 48824. IMMUNOLOGICAL INVESTIGATIONS, 1994 Aug
23;4:5:293-311. Journal code: 850462P. ISSN: 0892-1139. Pub. country:
United States. Language: English.

AB The potential role of B-1 cells i.e. the CD5+ B cell and "sister" B cell
subsets in autoimmunity is controversial. CD5+ B cells have been shown to
secrete **antibodies** of similar specificity as those found in many
systemic autoimmune diseases; in addition, increases in CD5+ B cell
frequency have been reported in patients suffering from rheumatoid
arthritis, Sjogren's syndrome, myasthenia gravis, insulin-dependent
diabetes mellitus and Hashimoto's thyroiditis. Whether these increases are
due to expansion of B-1 lineage cells in the human or due to
activation-induced expression of CD5 by conventional B cells is unclear.
In the present study, we used three murine models of systemic
autoimmunity: murine Acquired Immunodeficiency syndrome (MADS), chronic
graft-versus-host disease (GVHD), and collagen-induced arthritis (CIA) to
determine whether increases in B-1 cell frequency are universally seen in
models of autoimmunity which are mechanistically distinct. In contrast to
the aforementioned human systemic autoimmune diseases which exhibit an

increase in CD5+ B cell frequency, the percentage of CD5+ B cells declined in all three murine models of systemic autoimmune disease. Even though there was a decrease in the frequency of CD5+ B cells there was no change in the actual number of CD5+ B cells. Thus, the apparent decline in CD5+ B cell frequency was due to increases in either T cells, conventional Fc epsilon R+ B cells, or both. The only actual decline in a B cell subset was the loss of IgM+, Fc epsilon Rnull cells in both the spleen and peritoneal cavity of mice undergoing a chronic graft-versus-host reaction. Therefore, our data suggests that expansion of the B-1 subset does not occur as a general feature of murine systemic autoimmune disease. These observations, consistent with previous studies of Ig gene usage in autoreactive **antibodies**, support the view that expansion and differentiation of the CD5+ B cell subset is not a central event leading to autoantibody production.

L26 ANSWER 16 OF 37 MEDLINE DUPLICATE 9
94045239 Document Number: 94045239. PubMed ID: 8228625. Cytotoxic cell proteinase gene expression and cytolytic activity by anti-CD3-activated cytotoxic T lymphocytes is sensitive to cyclosporin A but is not dependent on interleukin-2 synthesis. Kaiser M; Brooks-Kaiser J; Fitzpatrick L; Bleackley R C; Hoskin D W. (Department of Microbiology and Immunology, Dalhousie University, Halifax, Nova Scotia, Canada.) JOURNAL OF LEUKOCYTE BIOLOGY, (1993 Nov) 54 (5) 458-64. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB We have examined the role of interleukin (IL) 2 in the expression of cytotoxic cell proteinases (CCP) 1 and 2, as well as in the induction of major histocompatibility complex (MHC)-unrestricted cytotoxic activity in murine T cell cultures following stimulation with anti-CD3 monoclonal **antibody**. A dramatic reduction in CCP-1 and CCP-2 gene expression and near absence of cytolytic activity was shown to occur in these cultures when the expression of IL-2 was inhibited by 10(-6) M cyclosporin A (CsA). The inhibitory effect of CsA could not be eliminated by the addition to culture of recombinant IL-2 at concentrations typically present in anti-CD3-stimulated T cell culture supernatants. Furthermore, when endogenous IL-2 (45-60 U/ml) present in anti-CD3-stimulated T cell cultures was neutralized with anti-mouse IL-2 **antibody** there was no effect on CCP-1 and CCP-2 mRNA expression and only a slight decrease in cytolytic activity. The expression of CCP-1 and CCP-2 gene products and the induction of MHC-unrestricted cytotoxic activity in anti-CD3-stimulated T cell cultures therefore occur independently of IL-2 synthesis but are regulated by a CsA-sensitive mechanism.

L26 ANSWER 17 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
93:126212 The Genuine Article (R) Number: KP121. COMPARISON OF THE INDUCTION OF ENDOTOXIN TOLERANCE IN PERITONITIS BY MONOPHOSPHORYL LIPID-A AND LIPOPOLYSACCHARIDE. ASTIZ M E Reprint ; SAHA I C; BROOKS K; CAREFATI C M; RACKOW E C. ST VINCENTS HOSP & MED CTR, NEW YORK MED COLL, DEPT MED, 133 W 11TH ST, NEW YORK, NY, 10031 Reprint. CIRCULATORY SHOCK MAR 1993 Vol. 39, No. 3, pp. 184-188. ISSN: 0990-6218. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND ALL FORMATS

AB We compared the induction of endotoxin tolerance with Salmonella minnesota monophosphoryl lipid A (MPL), a nontoxic derivative of lipid A, and S. minnesota endotoxin (LPS) in lethal endotoxemia and peritonitis. Lethal endotoxemia was induced by injecting 750 mug mouse LPS intravenously. Cerebral ligation and perforation was used to induce peritonitis. Tumor necrosis factor (TNF) was measured by immunoassay at 3 hr after lethal endotoxin infusion and 24 hr after peritonitis. A dose of 0.1 mug mouse of MPL or LPS significantly reduced endotoxin mortality from 100% to 50% and 0%, respectively (P < 0.05). The LPS for a 0.1 mug dose of MPL was 750 mug of LPS and the LPS for a 0.1 mug dose of LPS was 115 mug of endotoxin (P < 0.05). TNF levels decreased linearly when increasing doses of MPL and LPS were used to induce tolerance. At higher pretreatment

doses of LPS, survival benefits were attenuated despite the reduction in TNF levels. A 25 mg/kg dose of LPS reduced mortality from peritonitis from 93 to 45% ($P < 0.05$). Although MPL reduced short-term mortality, overall mortality was not significantly reduced despite using large doses of MPL. TNF levels peaked at 24 hr and were significantly lower than those following lethal endotoxemia. The induction of endotoxin tolerance by LPS and MPL is dose dependent, and LPS is modestly more effective in inducing endotoxin tolerance than MPL. Both LPS and MPL are significantly less effective in protecting against lethality from peritonitis.

116 ANSWER 19 OF 37 MEDLINE DUPLICATE 10
 94996351 Document Number: 94996351. PubMed ID: 9271238. Inhibition of DNA synthesis and IL-2 bioactivity in MLR by splenic pregnancy-associated natural suppressor cells involves the production of a TGF-beta 1-like molecule and a second distinct inhibitory factor. **Brooks-Kaiser J C**; Hoskin D W. (Department of Microbiology and Immunology, Dalhousie University, Halifax, Nova Scotia, Canada.) JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1993 Sep) 25 (1) 31-45. Journal code: 8001906. ISSN: 0165-0378. Pub. country: Ireland. Language: English.

AB Natural suppressor cells exhibiting a double-negative, immature T cell phenotype have been identified in maternal spleen during syngeneic murine pregnancy. In the present study, splenic pregnancy-associated natural suppressor (SPANS) cells are shown to express alpha/beta T cell receptors. SPANS cell-mediated inhibition of DNA synthesis by spleen cells responding in mixed lymphocyte reactions (MLR) is associated with a reduction in interleukin (IL)-2 bioactivity beginning after 96 h of culture. Although culture supernatants from suppressed MLR exhibit diminished ability to support the growth of IL-2-dependent CTLL-2 cells, SPANS cells themselves are unable to inhibit IL-2-driven CTLL-2 proliferation, suggesting that SPANS cells down-regulate IL-2 synthesis in MLR. IL-2 utilization in MLR is also inhibited by SPANS cells, since the addition of exogenous IL-2 fails to relieve the inhibitory effect of SPANS cells on lymphoproliferative responses in MLR. Flow cytometric analysis reveals that MLR performed in the presence of SPANS cells contain normal percentages of CD4 and IL-2 receptor-bearing spleen cells. Thus, SPANS cells do not inhibit cellular proliferation in MLR by selectively interfering with clonal expansion of IL-2-producing helper T cells or by down-regulating IL-2 receptor expression. We have determined that SPANS cells inhibit DNA synthesis in MLR via the production of a transforming growth factor (TGF)-beta 1-like suppressor factor, since cellular proliferation in MLR is restored to normal levels in the presence of anti-TGF-beta 1 neutralizing antibody. However, IL-2 bioactivity in these cultures remains low in comparison to control MLR, suggesting the presence of a second distinct suppressor factor. Although the identity of this second inhibitory molecule has yet to be determined, neutralizing antibody studies have ruled out IL-10.

116 ANSWER 19 OF 37 MEDLINE DUPLICATE 11
 92308750 Document Number: 92308750. PubMed ID: 1535357. Soybean agglutinin-positive natural suppressor cells in mouse bone marrow inhibit interleukin 2 production and utilization in mixed lymphocyte reactions. Hoskin D W; Bowser D A; **Brooks-Kaiser J C**. Department of Microbiology, Dalhousie University, Halifax, Nova Scotia, Canada. JOURNAL OF LEUKOCYTE BIOLOGY, 1990 Jun 51: 649-56. Journal code: 9456029. ISSN: 0741-5410. Pub. country: United States. Language: English.

AB Although natural suppressor (NS) cells resident in bone marrow (BM) have been the subject of intensive study, the exact nature and mode of action of these potentially important immunoregulatory cells are still uncertain. Here we show that NS cells with potent inhibitory effects on mixed lymphocyte reactions (MLRs) can be isolated from BM of normal adult mice by agglutination with the plant lectin soybean agglutinin (SBA). Complement-dependent lysis of SBA receptor-bearing BM cells with antibodies to asialoGM1, Mac-1, Thy-1.2, CD45, and L31

phenotypic markers reveals the presence of at least two distinct populations of BM NS cells. Most of the SBA-binding BM cells with NS capacity have the null phenotype and resemble hematopoietic stem cells, and some inhibitory SBA+ BM cells express the ZC1 marker found on pregnancy-associated splenic NS cells and the J11d.2 antigen characteristic of B cells and immature T cells. Results of positive selective experiments confirmed these findings. The mechanism of natural suppression has also been studied. Evidence is presented that SBA+ BM cells exert NS activity in MLRs by interfering with the production and utilization of interleukin 2. Indomethacin does not relieve natural suppression associated with SBA+ BM cells, indicating that prostaglandin synthesis is not a requirement for inhibitory function. However, neutralizing **antibodies** to transforming growth factor beta (TGF-beta) partially reverse the suppression mediated by SBA+ BM cells, suggesting that some BM NS cells may act through the release of an immunosuppressive molecule related to TGF beta.

L26 ANSWER 20 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
92:542319 The Genuine Article (R) Number: JM219. CD5 EXPRESSION IS MODULATED AS THE B-CELL MOVES THROUGH THE CELL-CYCLE. **BROOKS K H (Reprint)**; YOL Y S; PESTRA J J. MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint). ANNALS OF THE NEW YORK ACADEMY OF SCIENCES (04 MAY 1992) Vol. 651, pp. 259-260. ISSN: 0077-8923. Pub. country: USA. Language: ENGLISH.

L26 ANSWER 21 OF 37 MEDLINE DUPLICATE 12
92299374 Document Number: 92299374. PubMed ID: 1535063. Reactivity of monoclonal **antibody** 1E5.B5 with a novel phenotypic marker expressed on a murine natural suppressor cell subset. Hoskin D W; **Brooks-Kaiser J C**; Kaiser M; Murgita R A. (Department of Microbiology, Dalhousie University, Halifax, Nova Scotia.) HYBRIDOMA, (1992 Apr) 11 (2) 203-15. Journal code: 8202424. ISSN: 0272-457X. Pub. country: United States. Language: English.

AB Natural suppressor (NS) cells are antigen-nonspecific, MHC-independent immunoregulatory cells that are typically found in murine bone marrow (BM), newborn (NB) mouse spleen, and in splenic tissue of adult mice during pregnancy and following cyclophosphamide (CY) treatment. There has been a pressing need for the development of NS cell-specific monoclonal **antibodies** (mAb) since NS cells are generally described as null cells which lack the usual phenotypic markers of mature T cells, B cells, and macrophages. Here we present evidence that mAb 1E5.B5, which was raised in rats against murine splenic pregnancy-associated NS (SPANS) cells, recognizes a unique antigenic marker expressed by some, but not all, murine NS cells. In the presence of complement, mAb 1E5.B5 effectively eliminates SPANS activity, and diminishes NS activity of CY-treated spleen cells in mixed lymphocyte reactions (MLR). However, cytotoxic pretreatment with mAb 1E5.B5 had minimal effects on NS activity of BM and NB spleen cells. We also show that pregnancy spleen cells and CY-spleen cells with moderate NS activity in MLR can be positively selected for by "panning" with mAb 1E5.B5. In contrast, only weakly inhibitory cells are isolated from BM and NB spleen by this procedure. Cellular ELISA and flow cytometry confirm that mAb 1E5.B5 has specificity for pregnancy spleen cells and CY-spleen cells, as well as for NB spleen and BM cell preparations. Western blot analysis reveals that mAb 1E5.B5 reacts with a novel 55 kDa NS cell-associated antigen which we have termed NS-1. The NS-1 antigen is not present on other null cells such as natural killer (NK) cells and natural cytotoxic (NC) cells since cytotoxic pretreatment of pregnancy spleen cells with mAb 1E5.B5 does not affect **antibody**-dependent cell-mediated cytotoxicity, NK or NC activity.

L26 ANSWER 22 OF 37 MEDLINE
92299375 Document Number: 92299375. PubMed ID: 1535064. IL-2 and IL-6 Both Induce mRNAs and J Chain mRNA in a Clonal B Cell Line, but Differ in

their cell-cycle dependency for optimal signaling. Takayasu H; Brooks K H. Genetics Program, Michigan State University, East Lansing 48824. CELLULAR IMMUNOLOGY, 1991 Sep 136 (2): 472-85. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

AB We have found that a neoplastic Lyl+ B cell clone BCL1-3B3 can be stimulated to secrete IgM by a Th1-derived cytokine, IL-2, and/or by a Th2-derived cytokine, IL-5. At suboptimal concentrations these interleukins acted synergistically to enhance IgM secretion. Both IL-2 and IL-5 induced increases in microsecond and J chain mRNA levels. In the presence of both ILs, increases in microsecond and J chain mRNA were additive and paralleled increases in IgM secretion. Using cells synchronized at the G1/S border with excess thymidine or in early G1 using isoleucine-deficient media, IL-2 and IL-5 differed in their cell-cycle dependency for signal transmission. IL-5 appeared to act preferentially in late G1 of the cell cycle. In contrast, IL-2 stimulated S and G2 phase cells slightly more efficiently than cells in G1 of the cell cycle. Furthermore, a twofold increase in high-affinity IL-2R was observed as the cells entered S phase. The results suggest that although IL-2 and IL-5 can independently and additively induce differentiation of the Lyl+ BCL1-3B3 cells, they differ in their point of action during the cell cycle.

L26 ANSWER 23 OF 37 MEDLINE
91007479 Document Number: 91007479. PubMed ID: 2145206. Elevated membrane IgA+ and CD4+ (T helper) populations in murine Peyer's patch and splenic lymphocytes during dietary administration of the trichothecene vomitoxin (deoxynivalenol). Pestka J J; Dong W; Warner R L; Rascoy L; Bondy G S; Brooks K H. (Department of Food Science and Human Nutrition, Michigan State University, East Lansing 48824.) FOOD AND CHEMICAL TOXICOLOGY, (1990 Jun) 28 (6) 409-20. Journal code: 8207483. ISSN: 0278-6915. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Recent investigations indicate that dietary exposure to the trichothecene vomitoxin increases total and antigen-specific serum immunoglobulin A (IgA) and glomerular IgA accumulation in mice. In this study, the effects of 25 ppm dietary vomitoxin on the histological and lymphocytic profile of component immune organs in the mucosal lymphocyte migratory pathway were evaluated in the B6C3F1 mouse. Vomitoxin administration resulted in marked stimulation of the size and frequency of germinal centres in Peyer's patches, mesenteric lymph nodes and the spleen. A slight increase in the percentage of B cells in the Peyer's patch was observed, although vomitoxin treatment had no effect on the percentage of B cells in the spleen. The percentage of IgA+ cells in Peyer's patches and spleen were approximately twice that of controls at 4, 8 and 12 wk of vomitoxin exposure whereas the percentage of IgG+ cells decreased in these two organs. Exposure to vomitoxin increased the percentage of T cells in Peyer's patches and the spleen. The percentage of CD4+ cells (T helper subsets) increased slightly in Peyer's patches and more markedly (30-50%) in the spleen following vomitoxin treatment. Contrastingly, there was only a slight increase in the percentage of CD8+ cells (T cytotoxic/suppressor subset) in the spleens of vomitoxin-treated mice in comparison with controls, and no effect in Peyer's patches. The relative effects of vomitoxin on these two T cell populations was also reflected in increased CD4+: CD8+ ratios in Peyer's patches and spleen. These results are consistent with the hypothesis that dietary vomitoxin modulates normal regulation of the IgA response at the Peyer's patch level and that this is manifested in an altered lymphocyte distribution pattern in both the mucosal and systemic compartment. Notably increased levels of IgA+ and CD4+ cells are indicative of IgA-producing progenitors and T helper subsets, respectively, that in tandem could favour IgA hyperproduction and elevated IgA in serum.

L26 ANSWER 24 OF 37 SCISEARCH COPYRIGHT 1991 ISI B
91007479 The Genuine Article. P. Number: 91007479. CHARACTERIZATION OF A NEOPLASTIC B-CELL CLONE THAT SECRETES IgM IN RESPONSE TO TH1-DERIVED

LYMPHOKINES. **BROOKS K H (Reprint); OAKLEY C S; TAKAYASU H.**
MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint).
JOURNAL OF MOLECULAR AND CELLULAR IMMUNOLOGY 1990 Vol. 4, No. 6, pp.
339-348. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recent advances of T cell cloning have allowed the classification of T helper cells in terms of the lymphokines they secrete. The functional significance of segregating lymphokine production to unique T cell subsets is still being evaluated, but undoubtedly plays a key role in the regulatory mechanisms of the immune system. Initial studies have indicated that the Th₁ cells which secrete IL-2 and IFN-gamma may be primarily responsible for augmenting cell-mediated responses, whereas Th₂ cells, which release IL-4, IL-5, and IL-6, provide help for humoral responses. However, it is also known that B cells can respond to both IL-2 and IFN-gamma. This raises the question of the homogeneity of B lymphocyte activation requirements. Are all B cells responsive to all of the lymphokines with the end-result of stimulation depending largely on the relative concentrations of the various lymphokines, or are there B cell subsets which only respond to Th₁-derived lymphokines and others which respond to Th₂-derived lymphokines? Such differential activation requirements might be present to allow these subsets to play unique roles in immunological responses. Since B cell cloning techniques have not yet been developed to obtain a homogenous B cell population for studies of activation requirements, regulation of lymphokine receptors, and regulation of gene expression, we must utilize lymphokine-responsive neoplastic B cells. The vast majority of spontaneous B cell lymphomas appear to belong to a minor B cell subset which expresses the Lyl marker. This subset is clearly not representative of the majority of splenic B cells. In this report, we have characterized the lymphokine response pattern of Lyl-1 B cell clones derived from a spontaneous tumor occurring in an AKR mouse.

Neoplastic B cell clones were generated from the 225 lymphoma, which secrete significant levels of IgM upon stimulation with lymphokines produced by type 2 T helper (Th₂) cells. The 225 clones expressed a high-density of mIgM, varying densities of mIgD, and were mIgG and Lyl negative. Th₂-derived lymphokines found in D10.G4.1 SN will induce differentiation, as indicated by release of IgM in the culture SN. The 225 cells did not respond to IL-2, IFN-gamma, IL-1, or any combination of these lymphokines. Optimal differentiation occurred only when IL-4, IL-5, and IL-6 were present. The order of differentiative activity of these lymphokines was IL-5 > IL-4 > IL-6. The lack of IL-2 responsiveness in the face of IL-2R-alpha (p55) chain expression was due to the lack of high-affinity IL-2 receptors. In contrast, the IL-2 responsive clone BCL1-3B3 expresses approximately 950 high affinity IL-2R per cell. Thus, the 225-11 clone should provide a useful model system for the evaluation of the regulation of immunoglobulin gene expression mediated by Th₂-derived lymphokines.

126 ANSWER 25 OF 37 SCISEARCH COPYRIGHT 2000 ISI P
91258713 The Genuine Article R Number: F0150. ADRENOCORTICOTROPIN ACTH-
FUNCTIONS AS A LATE-ACTING B-CELL GROWTH-FACTOR AND SYNERGIZES WITH
INTERLEUKIN-5. **BROOKS K H (Reprint).** MICHIGAN STATE UNIV, DEPT
MICROBIOL, E LANSING, MI, 48824 (Reprint). JOURNAL OF MOLECULAR AND
CELLULAR IMMUNOLOGY 1990 Vol. 4, No. 6, pp. 327-337. Pub. country: USA.
Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In recent years there has been considerable discussion of possible cross-regulatory mechanisms involving the immune system and the neuroendocrine system. Certainly, evidence of hormonal communication between these two systems would provide at least a partial explanation for the many anecdotal observations of physical and mental stress affecting disease course. In previous studies of a neoplastic lymphokine-responsive B cell clone, BCL1-3B3, we noted that these cells produced a lymphokine

which could affect normal B cell growth and viability. Physical characterization of this lymphokine indicated that its molecular weight was identical to that of the neuroendocrine hormone adrenocorticotropin (ACTH). Since Blalock and colleagues had reported the production of ACTH by virally-infected B cells, we have investigated whether ACTH can functionally mimic the BCL1-3B3-derived lymphokine. The neuroendocrine hormone adrenocorticotropin (ACTH) can increase in vitro murine B lymphocyte proliferation when added at physiologically relevant concentrations between 10^{-9} to 10^{-11} M. ACTH does not mimic the action of any lymphokine known to be required for B cell proliferation such as IL-3, IL-4, or IL-5. ACTH requires the presence of one or more of these known B cell stimulatory factors for its action and the most marked increase in B cell proliferation were noted in assays for IL-5 activity where 10^4 - 10^5 M ACTH increased thymidine incorporation up to five-fold. Using two-stage assays, we determined that ACTH acts during the latter stages of B cell activation (i.e., 3-4 days after initial stimulation with either the combination of IL-4, GAMIG-Sepharose, and IL-1 or the combination of DnS and IL-5). These data indicate a direct role for a stress-induced neuroendocrine hormone in modulating the course of a humoral immune response.

L26 ANSWER 26 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1987:262595 Document No.: BR33:4491. INTERLEUKIN-2 INDUCES IGM SECRETION IN LYL+ NEOPLASTIC B CELLS BCL-1. **BROOKS K H**; KRAMMER P H; UHR J W; VITETTA E S. DEP. MICROBIOL., UNIV. TEX. HEALTH SCI. CENTER, SOUTHWESTERN MED. SCH., DALLAS, TEX. 75235.. GOLDSTEIN, G., J.-F. BACH AND H. WIGZELL (ED.). UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY NEW SERIES, VOL. 41. IMMUNE REGULATION BY CHARACTERIZED POLYPEPTIDES; STEAMBOAT SPRINGS, COLORADO, USA, JANUARY 25-FEBRUARY 1, 1986. XXVI+786P. ALAN R. LISS, INC.: NEW YORK, NEW YORK, USA. ILLUS. (1987) 0 (0), 305-314. CODEN: USMBD6. ISSN: 0735-9543. ISBN: 0-8451-2640-7. Language: English.

L26 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2002 ACS
1987:174381 Document No. 106:174381 Interleukin-2 induces IgM secretion in Lyl+ neoplastic B cells (BCL1). **Brooks, Kathryn H.**; Krammer, Peter H.; Uhr, Jonathan W.; Vitetta, Ellen S. (Southwest. Med. Sch., Univ. Texas, Dallas, TX, 75235, USA). UCLA Symp. Mol. Cell. Biol., New Ser., Volume Date 1986, 41:Immune Regul. Charact. Polypept., 305-14 (English) 1987. CODEN: USMBD6. ISSN: 0735-9543.

AB Cells from 2 neoplastic B cell clones have been used to exam. the effect of interleukin-2 (IL-2) on B cell differentiation. Cells from both clones express high levels of secretory IgM but relatively little secretory IgD; however, they differ in their expression of the Lyl marker. The cells from the Lyl+ BCL1-derived (BALB/c) clone secrete IgM in response to purified and recombinant IL-2. This response can be blocked with monoclonal anti-IL-2 antibodies. In contrast, cells from a Lyl- neoplastic B cell clone from AKR mice (AKR-225) do not differentiate in response to IL-2 or IL-2 plus recombinant interferon. The cells from both the BCL1 clone and the AKR-225 clone can differentiate in response to B cell stimulatory factors present in supernatants (SNs) of the alloreactive T cell line, EM 7.1. This EM 7.1 SN lacks significant IL-2 activity but does contain the differentiation factor for IgM. The different activation requirements of these Lyl+ and Lyl- neoplastic B cells is intriguing in light of both the assoc. of normal Lyl+ B cells with autoimmune disease and the prodn. of a B cell growth factor by the Lyl+ BCL1 clone but not the AKR-225 clone.

L26 ANSWER 28 OF 37 MEDLINE DUPLICATE 13
1987:174381 Document Number: 87-14946. PubMed ID: 2945963. Recombinant IL-2 but not recombinant interferon-gamma stimulates both proliferation and IgM secretion in a Lyl+ clone of neoplastic murine B cells (BCL1). **Brooks K H**; Vitetta E S. JOURNAL OF IMMUNOLOGY, 1986 Nov 15; 137

- 100 3205-10. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
- AB We have used a lymphokine-responsive clone (3B3) of B leukemia cells (BCL1) to examine the effects of several recombinant and purified lymphokines. Cells from BCL1-3B3 were induced to secrete IgM in the presence of recombinant interleukin 2 (rIL 2) (10 to 50 U/ml); a concomitant increase in proliferation was observed. Recombinant interferon-gamma (rIFN-gamma) was a potent inhibitor of proliferation. In addition, rIFN-gamma did not induce an increase in IgM secretion and, when added to rIL 2-stimulated BCL1-3B3 cells, completely blocked IgM secretion at a concentration of 10 U/ml. Purified and recombinant IL 1 (rIL 1) had no significant effect on differentiation either alone or in combination with rIL 2 and/or rIFN-gamma. However, rIL 1 was able to synergize with rIL 2 in enhancing the proliferation of BCL1-3B3. The ability of cells to respond to rIL 2 was limited to the in vitro (Ly-1+) clones of BCL1 cells since the in vivo derived (Ly-1-) BCL1 cells did not differentiate in response to IL 2. Consistent with their functional response to rIL 2, cells from the in vitro clone (3B3) are IL 2-receptor-positive (IL-2R+) and the in vivo derived BCL1 cells are IL-2R-. A second set of neoplastic B cell clones derived from the AKR 225 lymphoma did not respond to rIL 2 even though they expressed receptors for IL 2 and could be induced by T cell supernatant to secrete IgM, thus indicating that expression of IL 2R is not the sole requirement for IL 2 responsiveness. The monoclonal anti-IL 2R antibody (7D4) mimicked IL 2 in its ability to stimulate differentiation of BCL1-3B3 cells. These data suggest that rIL 2 and the monoclonal anti-IL-2R antibody are capable of inducing a differentiative response in the Ly-1+ BCL1-3B3 cells that is functionally equivalent to the response evoked by the previously described lymphokine B cell differentiation factor for IgM (BCDF mu). Thus, two distinct lymphokines appear to be providing a similar signal to a clonal neoplastic B cell population. Furthermore, rIL 2 is capable of providing both a proliferative and a differentiative signal.
- L26 ANSWER 29 OF 37 MEDLINE
85081355 Document Number: 85081355. PubMed ID: 3871214. Cell cycle-related expression of the receptor for a B cell differentiation factor. **Brooks K H**; Uhr J W; Vitetta E S. JOURNAL OF IMMUNOLOGY, (1985 Feb) 134 (2) 742-7. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
- AB Cloned, neoplastic B cells (BCL1) have been used to evaluate the expression of the receptor for the B cell differentiation factor, BCDF mu. These cells do not secrete IgM before stimulation with BCDF mu-containing T cell supernatants (SN). By inducing cell cycle synchrony in this homogeneous population, the expression of the BCDF mu receptor could be evaluated as a function of the cell cycle. Responsiveness to BCDF mu-containing SN is maximal when the cells are in S and G2 phases of the cell cycle, and a 2-hr exposure of cells to BCDF mu-containing SN during S/G2 results in optimal IgM secretion 5 days later. Cells in S/G2 are also maximally effective in absorbing BCDF mu activity from SN. These data support the hypothesis that B cells do not respond to differentiative signals until after they are committed to at least one round of cell division.
- L26 ANSWER 30 OF 37 EMBASE COPYRIGHT 1985 ELSEVIER SCI. B.V.
84141119 EMBASE Document No.: 184141119. T cell-derived lymphokines that induced IgM and IgG secretion in activated murine B cells. **Vitetta E S**; **Brooks K**; Chen Y-W; et al. Department of Microbiology, University of Texas Health Science Center, Dallas, TX 75395, United States. Immunological Reviews VOL 98 - 157-167 1984.
JCEIN: IMMEDI. Pub. Country: Denmark. Language: English.
- AB We have defined 2 lymphokine activities, termed BCDF.mu and BCDF.gamma, which are present in the supernatants of T cell tumors, lines and hybridomas. These lymphokines appear to act directly on activated normal B

cells or in the case of BCGF.mu., on BCL1 cells as well, to induce the synthesis and secretion of IgM or IgG1, respectively. These lymphokines are different from each other as well as from IL-1, IL-2, IFN.gamma., and conventional TRF. By molecular weight, BCGF.mu. is different from BCGF. The 2 BCGFs appear to bind to 2 different receptors on the cell surface and, thereby, to induce changes in the levels of isotype-specific mRNA and secreted immunoglobulin. The binding of BCGF.mu. to target cells appears to be cell-cycle related, optimal in G2S, and independent of T cells and macrophages. This has not been proven for BCGF.gamma.. It is possible that a subset of cells present in normal B cell populations, but not represented by the cloned BCL1 cells, is needed for BCGF.gamma. activity. Studies from other laboratories describing BCGF.gamma. (Severinson et al. 1982) BCGF.alpha. (Mayer et al. 1982, Kawanishi et al. 1983), and BCGF.epsilon. (Kishimoto & Ishizaka 1973, Hirashima et al. 1981), activities in T cell supernatants suggest that T cell-derived lymphokines may regulate the expression and/or secretion of several classes of immunoglobulin in activated B cells.

L26 ANSWER 31 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1984:44777 Document No.: BR26:44777. LYMPHOKINE INDUCED DIFFERENTIATION OF CLONAL NEOPLASTIC B CELLS. **BROOKS K**; YUAN D; UHR J; KRAMMER P; VITETTA E S. UNIV. TEX. HEALTH SCI. CENT. DALLAS, DALLAS, TEX. 75235.. 67TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, CHICAGO, ILL., USA, APRIL 10-15, 1983. FED PROC. (1993) 42 (5), ABSTRACT 6101. CODEN: FEPR7. ISSN: 0014-9446. Language: English.

L26 ANSWER 32 OF 37 MEDLINE DUPLICATE 14
83192467 Document Number: 83192467. PubMed ID: 6601774.
Lymphokine-induced IgM secretion by clones of neoplastic B cells. **Brooks K**; Yuan D; Uhr J W; Krammer P H; Vitetta E S. NATURE, (1983 Apr 28) 302 (5911) 825-6. Journal code: 0140462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The induction of **antibody** secretion by B cells requires T-cell-derived factors 1-5. Such factors have been described 1,2,6-12 but the precise relationship among these various factors is not clear, and it has been difficult to demonstrate that these factors act directly on the B cell and do not exert their effect via T cells or macrophages. In this report we describe the direct induction of IgM synthesis and secretion in cloned lines of long-term tissue culture adapted neoplastic B cells (BCL1) by T-cell supernatants from phorbol-12-myristate 13-acetate (PMA)-induced EL-4 cells or concanavalin A (Con A)-induced 7.1.1a cells 5,9. We have termed this activity BCGFmu (B-cell differentiation factor for IgM). The supernatants containing BCGFmu induce activated and neoplastic B cells to secrete IgM5 and the factor responsible is distinct from BCGF13, interleukin-3 (IL-3), the classical T-cell replacing factor TRF described by Schimpl and Wecker5, and immune interferon (IFN gamma) 5.

L26 ANSWER 33 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 15
83182564 EMBASE Document No.: 1983182564. The correlation between the activation state of B cells and their capacity for in vitro propagation of immunologic memory. **Brooks K.H.**; Feldbush T.L. Dep. Microbiol., Univ. Iowa, Iowa City, IA 52242, United States. Cellular Immunology 76:2 213-223 1983.
CODEN: CLIM89. Pub. Country: United States. Language: English.

AB The B-cell population responsible for in vitro antigen-mediated proliferation and expansion of the memory B-cell population is a large activated blast. Such cells predominate early after antigen priming and can be regenerated by adjuvant Bordetella pertussis stimulation in vivo. Although these cells are proliferating in vivo, additional stimuli are needed for expansion of the memory population in vitro. These triggering requirements include specific antigen (NP-GNA) and the assistance of adherent accessory cells. Although T cells are present in the culture,

their role in the propagation of memory is not completely clear. Using the unrelated antigen, sheep erythrocytes, we have shown that 'bystander' T-cell help can mediate differentiation of these memory B-cell blasts to AFC, but it cannot induce expansion of the memory-cell population. However, the fact that the TI-2 antigen DNP-Ficoll is a relatively ineffective inducer of memory-cell propagation inducing an expanded response which is less than 10% of that induced by the T-cell-dependent antigen, DNP-OVA, suggests that T cells may be involved, possibly via production of B-cell growth factor. Thus, the minimal requirements for triggering the propagation of B-cell memory include i) a blastogenic signal which can be mediated by adjuvant, ii. specific antigen, and iii. adherent accessory-cell help.

L26 ANSWER 34 OF 37 MEDLINE DUPLICATE 16
81265503 Document Number: 81265503. PubMed ID: 7021678. Generation of antibody-mediated regulation during in vitro clonal expansion of memory B lymphocytes. **Brooks K H**; Feldbush T L. JOURNAL OF IMMUNOLOGY, (1981 Sep) 127 (3) 963-7. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

L26 ANSWER 35 OF 37 MEDLINE
81265502 Document Number: 81265502. PubMed ID: 7021677. In vitro antigen-mediated clonal expansion of memory B lymphocytes. **Brooks K H**; Feldbush T L. JOURNAL OF IMMUNOLOGY, (1981 Sep) 127 (3) 959-63. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB An in vitro model for the propagation and expansion of the memory B lymphocyte population is described. DNP-BGG immune cells were mixed with OVA immune cells and challenged immediately with DNP-OVA. After the 1st response had begun to wane, the cells were rechallenged with DNP-OVA (day 11 of culture). An average of 13-fold more PFC were observed after delayed challenge (day 11). This expansion in the PFC response was an antigen-dependent process and did not involve recruitment of new memory cells from the virgin lymphocyte pool. The level of expansion of the memory cell pool was also calculated using limiting dilution analysis and was found to fall in a range of 16- to 67-fold increase in precursor frequency. In addition to the expansion of the memory B cell population, we also observed the development of 2 immunoregulatory cycles previously observed only in vivo. First, in the presence of persistent antigen, a cyclical PFC response was seen. Second, after day 10 of culture, optimal PFC numbers were observed only when DNP-lysine was added to the plaque assay. Such hapten-augmentable PFC responses have been reported by other investigators as indicative of anti-idiotypic regulation. This possibility is examined more extensively in the following communication.

L26 ANSWER 36 OF 37 CAPLUS COPYRIGHT 1981 ACS
1982:559252 Document No. 87458292 Isolation and characterization of an alpha-1-antitrypsin-related glycoprotein from human liver. **Glew, Robert H**; Zidian, J. L.; Chiao, J. P.; Fuhschmidt, T.; Iannarino, Richard M.; **Brooks, K. P.** (Sch. Med., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA). Electrophor. '81 [Eighty-One], Proc. Int. Conf., 3rd, 519-21. Editor s: Allen, Robert Chadbourne; Arnau, Philippe. de Gruyter: Berlin, Fed. Rep. Ger. English 1981. C05EN: 45N43.

AB A 68,000-dalton glycoprotein which cross-reacts with antibody to human plasma alpha-1-antitrypsin (A1) was purified from the 1,000-g supernatant of human liver. This glycoprotein (I-ORM) had 9.6% of the immunoreactivity of A1 and no antiprotease activity. Isolated, fucose-rich resolved I-ORM into 3 fractions which differed in immunoreactivity. Carbohydrate and amino acid analyses were carried out. I-ORM, which differed from A1 in mol. wt., also differed substantially in CNBr- and chymotrypsin-derived fragments. The basis of the relatedness of plasma A1 and I-ORM, which represents only approx. 1% of liver protein content, is not known; however, as immunospecificity was the major criteria for

purifn. the report of frequent findings of I-CRM in normal and diseased liver may be accounted for by the present observation.

126 ANSWER 37 OF 37 MEDLINE DUPLICATE 17
90132519 Document Number: 90132519. PubMed ID: 6153590. The generation of memory B-cell subpopulations capable of proliferation and expansion of the pool: effect of time and antigen. **Brooks K H**; Feldbush T L; van der Hoven A. CELLULAR IMMUNOLOGY, 198 Mar 15; 90:2: 390-404. Journal code: 1046405. ISSN: 0008-8749. Pub. country: United States. Language: English.

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L3 3 DUP REMOVE L2 3 DUPLICATES REMOVED.

=> d 13 1-3 cbib abs

L3 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
2002034456 Document Number: 21957817. PubMed ID: 11962725. Anti-CD23
monoclonal antibody inhibits germline Cepsilon transcription in B cells.
Yabuuchi Shingo; Nakamura Takehiko; Kloetzer William S
; Reff Mitchell E. (Seikagaku Corporation, Central Research
Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) .
Int Immunopharmacol. (2002 Mar) 2 (4) 453-61. Journal code: 100965259.
ISSN: 1567-5769. Pub. country: Netherlands. Language: English.
AB A chimeric macaque/human (PRIMATIZED) anti-CD23 antibody
, p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40
antibody-stimulated IgE production by human peripheral blood mononuclear
cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain
reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline
Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data
suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE
through the inhibition of germline Cepsilon RNA synthesis. Early addition
of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE
inhibition. In contrast, later addition of p6G5G1 still showed inhibition
of increased levels of surface CD23, which is normally upregulated by
stimulation with IL-4 and anti-CD40.

L3 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE
inhibition in B cells by anti-CD23 monoclonal antibodies is functionally
dependent on the immunoglobulin Fc domain. Nakamura T;
Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J;
Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E.
(Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.)
INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41.
Journal code: 7904795. ISSN: 0192-0561. Pub. country: ENGLAND: United
Kingdom. Language: English.
AB CD23, the low affinity receptor for IgE (FcepsilonRII), is involved in
regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies
to human CD23 were generated from cynomolgus macaques immunized with
purified soluble CD23 (sCD23). Four of the five primate antibodies blocked
the binding of IgE complexes to CD23 positive cells and also inhibited the
production of IgE in vitro by IL-4 induced human peripheral blood
mononuclear cells (PBMC). The variable domains of several primate
antibodies were utilized to construct chimeric macaque/human
PRIMATIZED R1 monoclonal antibodies. PRIMATIZED R1 p5E8G1,
containing human gamma 1 constant region, inhibited IgE production in
vitro as efficiently as the parent primate antibody, but the human gamma 4
constant version, PRIMATIZED R1 p5E8G4, was not as effective in IgE
inhibition. An F ab' 2 of p5E8G1 did not inhibit IgE production but did
interfere with IgE inhibition by the intact anti-CD23
antibody in a dose dependent fashion. The murine monoclonal
antibody MHM6 recognizes human CD23 at a different epitope than primate
antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with
the F ab' 2 of p5E8G1, the F ab' 2 of MHM6 also failed to inhibit IgE
production. These data imply that the mechanism by which anti-CD23
antibodies inhibit IgE production requires cross-linking of CD23
to an IgE receptor. These data also imply that neither bivalent
cross-linking of CD23 alone or inhibition of CD23 binding to its natural
ligands is sufficient to inhibit IgE production.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT LTD ADS

1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. **Reff, Mitchell R.**; Barnett, Richard Spence; McLachlan, Karen Petta Ideo Pharmaceuticals Corporation, USA. U.S. US 5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid Desmond. This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, Mela cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors (Molly) and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, N1+Neomycin phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human **CD23 antibody** and immunoadhesin in Desmond marked CHO cells was achieved.

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L1 15 CHIMERIC CD23

=> s 11 and antibod?
L2 6 L1 AND ANTIBOD?

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PROCESSING COMPLETED FOR L2
L3 2 DUP REMOVE L2 (4 DUPLICATES REMOVED)

=> d 13 1-2 cbib abs

L3 ANSWER 1 OF 2 MEDLINE DUPLICATE 1
2000384038 Document Number: 20304490. PubMed ID: 10845922. Engagement of
CD11b and CD11c beta2 integrin by **antibodies** or soluble CD23
induces IL-1beta production on primary human monocytes through
mitogen-activated protein kinase-dependent pathways. Rezzonico R;
Chicheportiche R; Imbert V; Dayer J M. (Division of Immunology and
Allergy, Clinical Immunology Unit (Hans Wilsdorf Laboratory), Department
of Internal Medicine, University Hospital, Geneva, Switzerland..
rezzonico@unice.it). BLOOD. 2000 Jun 15; 95 (12): 3668-77. Journal code:
7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.
AB beta2 integrins are involved in the recruitment of leukocytes to
inflammatory sites and in cellular activation. We demonstrate that
ligation of CD11b/Mac-1, CR3 or CD11c/p150, CR4 alpha chains of beta2
integrins by mAbs or soluble **chimeric CD23** sCD23 on
human freshly isolated monocytes rapidly stimulates high levels of
interleukin-1beta production. This induction takes place at the
transcriptional level and is regulated by members of the mitogen-activated
protein kinase (MAPK) family. Indeed, stimulation of monocytes through
engagement of CD11b or CD11c results in the phosphorylation and activation
of ERK1, ERK2, and p38 MAPK kinases. MEK1, a potent inhibitor of the
upstream activator of ERK1/2, ie, MEK1, suppresses IL-1beta messenger
RNA (mRNA) expression in a dose-dependent fashion, showing the implication
of this pathway in the transcriptional control of IL-1beta production. On
the other hand, inhibition of p38 by SB203580 indicates that this MAPK is
involved in the control of IL-1beta production at both transcriptional and
translational levels. Together these data demonstrate that ligation of

CD11b and CD11c beta2 integrins by mAbs or CD23 fusion proteins triggers the activation of 2 distinct MAPK signaling pathways that cooperate in controlling IL-1beta synthesis at different levels. (Blood. 2000;95:3869-3877)

L3 ANSWER 2 OF 2 SCISEARCH COPYRIGHT 2010 ISI P
1998;947017 The Genuine Article F Number: 146NG. Production of a chimeric form of CD23 that is oligomeric and blocks IgE binding to the Fc epsilon RI. Kelly A B; Chen B H; Woodward E C; Conrad D H. Reprint. VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, BOX 960678, MOV STN, RICHMOND, VA 23298. Reprint; VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, RICHMOND, VA 23298. JOURNAL OF IMMUNOLOGY (15 DEC 1998) Vol. 161, No. 12, pp. 6696-6704. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The low affinity receptor for IgE (Fc epsilon RI/CD23) has previously been shown to interact with IgE with a dual affinity. Three chimeric constructs were created containing the lectin domain (amino acids 172-188) or the 'neck' and lectin domain (amino acids 157-188) attached to subunits of oligomeric proteins. All chimeras were incapable of interacting with IgE with either a high or low affinity, indicating that the alpha-helical stalk of CD23 is important for orienting the lectin heads such that an interaction with IgE can occur. This concept received further support in that a **chimeric CD23** composed of the human CD23 stalk and the mouse CD23 lectin head bound mouse IgE with a dual affinity, but could only bind rat IgE with a low affinity. Effort was next concentrated on a construct consisting of the entire extracellular (EC) region of CD23. A mutation to the first cleavage site of CD23 (CIM) resulted in a more stable molecule as determined by a decrease of soluble CD23 release. A soluble chimeric EC-CIM was prepared by attaching an isoleucine zipper to the amino terminus (IzEC-CIM). The interaction with IgE by IzEC-CIM was found to be superior to that seen with EC-CD23. The IzEC-CIM could inhibit binding of IgE to both CD23 and the high affinity receptor for IgE, Fc epsilon RI, providing further evidence for a strong interaction with IgE. Fc epsilon RI inhibition (similar to 70%) was seen at equimolar concentrations of IzEC-CIM, implying the effectiveness of this chimera and suggesting its potential therapeutic value.

=> s humanized anti CD23
L4 1 HUMANIZED ANTI CD23

=> d 14 cbib abs

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
2000;457197 Document No. 133:5769 Enhanced proteins production in cell culture stimulated by unusually low alkaloid acid concentrations. Islam, Seema; Sharp, Nigel Alan. Glaxo Group Limited, UK. PCT Int. Appl. WO 2000035282 A1 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GR, GM, GU, HU, ID, IL, IN, JP, KE, KR, KZ, LG, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TC, UA, US, UG, UZ, VN, YU, ZA, ZW, AM, AC, BY, KG, KZ, MD, RU, TC, TM; RW: AT, BE, BF, BI, CF, CG, CH, CI, CM, CV, DE, DK, ES, FI, FR, GA, GB, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TL, TD. English. SCIENT. FIXXED. APPLICATION: WO 1999-081157 19991222. PRIORITY: GB 1999-18624 19991023.

AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkaloid acid or its salt at a maintained concn. of less than 100M. Thus, NSC cells transfected with an IgG1 humanized anti -CD23 antibody was cultured for 56 days in a draw and cell

repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in antibody prodn. over the control.

=> s monoclonal
L5 727044 MONOCLONAL

=> s 15 and human CD23
4 FILES SEARCHED...
L6 43 15 AND HUMAN CD23

=> s 16 and chimeric
L7 7 L6 AND CHIMERIC

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PROCESSING COMPLETED FOR L7
L8 3 DUP REMOVE L7 (4 DUPLICATES REMOVED)

=> d 18 1-3 cbib abs

L8 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:370946 Document No.: PREV200200370546. Antibodies against the stalk region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis. Caven, Timothy Hays (1); Ma, Check (1); Beavill, Rebecca; Beavill, Andrew; Ghirlando, Rodolpho; Gould, Hannah; Conrad, Daniel (1). (1) Virginia Commonwealth University, 1217 East Marshall Street, Richmond, VA, 23298 USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1239. <http://www.faseb.org/>. print. Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language: English.
AB The stalk region of human CD23 comprising a.a. 48-153 was expressed in E. coli and purified. In addition a chimeric human CD23 was prepared consisting of the extracellular region of CD23 linked to a modified leucine zipper (LZ-CD23). Polyclonal antisera were produced in rabbits and shown to block binding of IgE to CD23 both on cell surfaces as well as the interaction of LZ-CD23 with IgE in an ELISA based assay. The antisera was also shown to inhibit IgE synthesis in an anti-CD40/IL-4 stimulated human PBL model. The inhibition was dose dependent and essentially complete blockage of IgE production was seen at a relatively low dose of anti-stalk. FACS analysis using CD23+B lymphoblastoid cells indicated little if any endocytosis and/or protection from cleavage induced by the anti-stalk. Monoclonal antibodies against the human stalk have also been prepared and these are being analyzed for the capacity to inhibit IgE binding and IgE synthesis, as well as compare their efficacy to the anti-lectin mAbs. The results indicate that targeting the stalk region is efficacious with respect to blocking IgE production.

L9 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:186685 Document No.: PREV200200186685. Induction of apoptosis by IIEC-152 anti-CD23 in lymphoma cells. Pathan, Ruchat 1; Hariharan, Kandasamy 1; Hopkins, Michael; Saven, Alan; Peff, Mitchell 1; Hanna, Nabil 1; Grint, Paul 1. (1) IIEC Pharmaceuticals, San Diego, CA USA. Blood, November 16, 2001 Vol. 98, No. 11 Part 1, pp. 367a. <http://www.bloodjournal.org/>. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 1-6, 2001 ISSN: 0006-4971. Language: English.
AB IIEC-152 is a primatized monoclonal antibody to human CD23, the low-affinity receptor for IgE on B cells that has been implicated in the regulation of IgE synthesis. In vitro and in vivo data have demonstrated that IIEC-152 suppresses IgE synthesis. IIEC-152 is currently in clinical trials for use in allergic asthma. CD23 is also

expressed at high levels in certain B-cell malignancies, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a chimeric monoclonal antibody to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the treatment of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain CD23 positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab)₂ fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of approx 10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong antibody dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of CD23, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

L8 ANSWER 3 OF 3 MEDLINE DUPLICATE 1
2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcεγR2b), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED(R)) monoclonal antibodies. PRIMATIZED(R) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED F p5E8G4, was not as effective in IgE inhibition. An F(ab')₂ of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')₂ of p5E8G1, the F(ab')₂ of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-CD23 antibodies inhibit IgE production requires cross-linking of CD23 to an IgE receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligand is sufficient to inhibit IgE production.

END

FILE 'HOME' ENTERED AT 09:44:54 ON 04 JUL 2000

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:25:09 ON
04 JUL 2002
L1      15 S CHIMERIC CD23
L2      6 S L1 AND ANTIBOD?
L3      2 DUP REMOVE L2 4 DUPLICATES REMOVED
L4      1 S HUMANIZED ANTI CD23
L5      727044 S MONOCLONAL
L6      43 S L5 AND HUMAN CD23
L7      7 S L6 AND CHIMERIC
L8      3 DUP REMOVE L7 4 DUPLICATES REMOVED

=> s l5 and chimeric CD23
L9      1 L5 AND CHIMERIC CD23

=> d l9 cbib abs

L9      ANSWER 1 OF 1      MEDLINE
2000384038 Document Number: 20304490.      PubMed ID: 10845922.      Engagement of
CD11b and CD11c beta2 integrin by antibodies or soluble CD23 induces
IL-1beta production on primary human monocytes through mitogen-activated
protein kinase-dependent pathways. Rezzonico R; Chicheportiche R; Imbert
V; Dayer J M. (Division of Immunology and Allergy, Clinical Immunology
Unit (Hans Wilsdorf Laboratory), Department of Internal Medicine,
University Hospital, Geneva, Switzerland.. rezzonico@unice.it) . BLOOD,
(2000 Jun 15) 95 (12) 3868-77.      Journal code: 7603509. ISSN: 0006-4971.
Pub. country: United States. Language: English.
AB      beta2 integrins are involved in the recruitment of leukocytes to
inflammatory sites and in cellular activation. We demonstrate that
ligation of CD11b (Mac-1, CR3) or CD11c (p150, CR4) alpha chains of beta2
integrins by mAbs or soluble chimeric CD23 (sCD23) on
human freshly isolated monocytes rapidly stimulates high levels of
interleukin-1beta production. This induction takes place at the
transcriptional level and is regulated by members of the mitogen-activated
protein kinase (MAPK) family. Indeed, stimulation of monocytes through
engagement of CD11b or CD11c results in the phosphorylation and activation
of ERK1, ERK2, and p38/SAPK2 MAP kinases. U0126, a potent inhibitor of the
upstream activator of ERK1/2, ie, MEK1/2, suppresses IL-1beta messenger
RNA (mRNA) expression in a dose-dependent fashion, showing the implication
of this pathway in the transcriptional control of IL-1beta production. On
the other hand, inhibition of p38 by SB203580 indicates that this MAPK is
involved in the control of IL-1beta production at both transcriptional and
translational levels. Together these data demonstrate that ligation of
CD11b and CD11c beta2 integrins by mAbs or sCD23 fusion proteins triggers
the activation of 2 distinct MAPK signaling pathways that cooperate in
controlling IL-1beta synthesis at different levels.      Blood.
2000;95:3868-3877.

=> s l5 and humanized CD23
L10     3 L5 AND HUMANIZED CD23

=> d l10

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FILE 'HOME' ENTERED AT 08:34:04 ON 24 JUL 2002

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:35:09 ON
24 JUL 2002
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L2      6 S L1 AND ANTIBOD?
L3      2 DUP REMOVE L2 4 DUPLICATES REMOVED
L4      1 S HUMANIZED ANTI CD23
L5      727044 S MONOCLONAL
L6      43 S L5 AND HUMAN CD23

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L17 7 S L6 AND CHIMERIC
 L8 3 DUP REMOVE L7 14 DUPLICATES REMOVED
 L9 1 S L6 AND CHIMERIC CD23
 L10 6 S L6 AND HUMANIZED CD23

=> s l6 and Ige
 L11 32 L6 AND IGE

=> dup remove l11
 PROCESSING COMPLETED FOR L11
 L12 17 DUP REMOVE L11 21 DUPLICATES REMOVED

=> d l12 1-17 chib abs

L12 ANSWER 1 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 2002:370946 Document No.: PREV200200370946. Antibodies against the stalk
 region of huCD23 block binding of **IgE** and inhibit in vitro
IgE synthesis. Caven, Timothy Hays (1); Ma, Check (1); Beavil,
 Rebecca; Beavil, Andrew; Ghirlando, Rodolpho; Gould, Hannah; Conrad,
 Daniel (1). (1) Virginia Commonwealth University, 1217 East Marshall
 Street, Richmond, VA, 23298 USA. FASEB Journal, (March 22, 2002) Vol. 16,
 No. 5, pp. A1239. <http://www.fasebj.org/>. print. Meeting Info.: Annual
 Meeting of Professional Research Scientists on Experimental Biology New
 Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language:
 English.

AB The stalk region of **human CD23** comprising a.a. 48-153
 was expressed in *E. coli* and purified. In addition a chimeric
human CD23 was prepared consisting of the extracellular
 region of CD23 linked to a modified leucine zipper (LZ-CD23). Polyclonal
 antisera were produced in rabbits and shown to block binding of
IgE to CD23 both on cell surfaces as well as the interaction of
 LZ-CD23 with **IgE** in an ELISA based assay. The antisera was also
 shown to inhibit **IgE** synthesis in an anti-CD40/IL-4 stimulated
 human PBL model. The inhibition was dose dependent and essentially
 complete blockage of **IgE** production was seen at a relatively low
 dose of anti-stalk. FACS analysis using CD23+B lymphoblastoid cells
 indicated little if any endocytosis and/or protection from cleavage
 induced by the anti-stalk. **Monoclonal** antibodies against the
 human stalk have also been prepared and these are being analyzed for the
 capacity to inhibit **IgE** binding and **IgE** synthesis, as
 well as compare their efficacy to the anti-lectin mabs. The results
 indicate that targeting the stalk region is efficacious with respect to
 blocking **IgE** production.

L12 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2002 ACS
 2001:747174 Document No. 135:287537 Inhibitors for the formation of soluble
human CD23 and their use in treatment of diseases.
 Frey, Juergen Germany. Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp.
 DESIGNATED STATES: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL,
 SE, MC, PT, IE, SI, LT, LV, FI, RO. English. CODEN: EPXXXX.
 APPLICATION: EP 2000-107515 20000407.

AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is
 described in which the overprodn. of sCD23 is implicated. This compn.
 comprises an inhibitor for the formation of human sol. CD23 which
 inhibitor decreases or blocks selectively the activity of the
 metalloprotease ALAMP which otherwise mediates the shedding of sCD23 in
 human B-cell lines. Also described is a pharmaceutical compn. wherein the
 inhibitor for the formation of human sol. CD23 is a **monoclonal**
 or polyclonal antibody directed against the metalloprotease ALAMP or
 wherein the inhibitor is an antisense oligonucleotide which is specific
 for p-myr. Such a pharmaceutical compn. may be used in a method for
 selectively inhibiting the formation of ALAMP as well as the formation of
 sCD23. It is a suitable medicament against inflammatory disorders,

autoimmune diseases and allergy.

L12 ANSWER 3 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:156685 Document No.: PREV200200156685. Induction of apoptosis by IDEC-152 anti-CD23 in lymphoma cells. Pathan, Nuzhat [1]; Hariharan, Kandasamy [1]; Hopkins, Michael; Saven, Alan; Peff, Mitchell [1]; Hanna, Nabil [1]; Grint, Paul [1]. 1. IDEC Pharmaceuticals, San Diego, CA USA. Blood, November 16, 2001 Vol. 98, No. 11 Part 1, pp. 367a.
<http://www.bloodjournal.org/>. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971. Language: English.

AB IDEC-152 is a primatized **monoclonal** antibody to **human CD23**, the low-affinity receptor for **IgE** on B cells that has been implicated in the regulation of **IgE** synthesis. In vitro and in vivo data have demonstrated that IDEC-152 suppresses **IgE** synthesis. IDEC-152 is currently in clinical trials for use in allergic asthma. CD23 is also expressed at high levels in certain B-cell malignancies, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a chimeric **monoclonal** antibody to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the treatment of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain CD23 positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab)2 fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of approx 10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong antibody dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of CD23, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

L12 ANSWER 4 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:320835 Document No.: PREV200000320835. Gamma-1 anti-**human CD23 monoclonal** antibodies. Peff, Mitchell E. [1]; Kloepper, William S.; Nakamura, Takehiko. 1. San Diego, CA USA. ASSIGNEE: IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6011138 January 04, 2000. Official Gazette of the United States Patent and Trademark Office Patents, Jan. 4, 2000 Vol. 1233, No. 1, pp. No pagination. e-file. ISSN: 0099-1133. Language: English.

AB Anti-**human CD23 monoclonal** antibodies containing human gamma 1 constant domains and therapeutic uses are provided. These antibodies inhibit IL-4 induced **IgE** production by B-cells significantly greater than antibodies containing other constant domains.

L12 ANSWER 5 OF 17 MEDLINE
2000:055573 Document Number: 055573. PubMed ID: 10649977. In vitro **IgE** inhibition in B cells by anti-CD23 **monoclonal** antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloepper W S; Brans E; Hariharan P; Chamat S; Cao W; LaBatre M S; Chinn P C; Morena F A; Skasnowsky W S; Li Y P; Chen A; Peff M E. Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.

INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 2000 Feb; 22: 2: 131-41.
Journal code: 7904759. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

- AB CD23, the low affinity receptor for IgE Fc ϵ 2R, is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED(R)) monoclonal antibodies. PRIMATIZED(R) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED(R) p5E8G4, was not as effective in IgE inhibition. An F(ab')₂ of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')₂ of p5E8G1, the F(ab')₂ of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-CD23 antibodies inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

L12 ANSWER 6 OF 17 MEDLINE

2000150237 Document Number: 20150237. PubMed ID: 10684962.

- Characterization of novel Fc ϵ 2R/CD23 isoforms lacking the transmembrane (TM) segment in human cell lines. Yoshikawa T; Matsui M; Gon Y; Yoshioka T; Hiramata M; Lynch R G; Naito K; Yodoi J. (Institute for Virus Research, Kyoto University, 53 Kawahara-cho, Sakyo-ku, Kyoto, Japan.) MOLECULAR IMMUNOLOGY, (1999 Dec) 36 (18) 1223-33. Journal code: 7905289. ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.
- AB Human Fc ϵ 2R/CD23 is an approximately 45 kDa type II transmembrane glycoprotein belonging to the C-type animal-lectin family, and has two isoforms (a and b) that only differ in their intracytoplasmic tails. We previously found that in several human and mouse cell lines there were two additional CD23 transcripts (a' and b') lacking the exon 3 that encodes the entire transmembrane segment and a part of cytoplasmic tails. In this study, we analyzed the putative CD23a' and CD23b' products at protein levels and characterized with rabbit polyclonal antibodies against novel amino-acid sequences of the putative CD23a' and CD23b' molecules. anti-CD23a' Ab, anti-CD23b' Ab. Western blots in COS cells transfected with CD23a' or CD23b' cDNA as well as in vitro translation assays showed that the a' and b' CD23 transcripts were translated to about 40 kDa molecules. These 40 kDa molecules were also recognized by a polyclonal antibody against 25 kDa soluble fragment of human CD23. We also found that human cells having mRNAs for CD23a' and CD23b' expressed protein products recognized specifically by anti-CD23a' or anti-CD23b' Ab, respectively. In addition, the CD23a' and CD23b' molecules in transfected COS cells were resistant to Endo H f and PNGase F, although these truncated forms as well as the membrane-associated forms had an asparagine residue responsible for the N-linked glycosylation. Taken together, our results show that the a' and b' CD23 transcripts are expressed and translated in human lymphoid cells and that their translated products are retained in the cytoplasm where they might play an unique regulatory role in the expression of the full-length CD23 on the cell surface.

disclosed. The antibodies are useful for modulating or inhibiting induced **IgE** expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced **IgE** prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L12 ANSWER 10 OF 17 MEDLINE DUPLICATE 4
97351082 Document Number: 97351082. PubMed ID: 9207459. Inhibition of apoptosis in a human pre-B-cell line by CD23 is mediated via a novel receptor. White L J; O'Garra B W; Graber P; Aubry J P; Bonnefoy J Y; Cushtley W. Institute of Biomedical & Life Sciences, University of Glasgow, Scotland, UK. BLOOD, 1997 Jul 1; 90 (1): 234-43. Journal code: 7603509. ISSN: 0006-4671. Pub. country: United States. Language: English.

AB Human CD23 is a 45-kD type II membrane glycoprotein, which functions as a low-affinity receptor for **IgE** and as a ligand for the CD21 and CD11b/CD11c differentiation antigens. CD23 is released from the surface of cells as soluble fragments, and a 25-kD species of soluble CD23 (sCD23) appears to act as a multifunctional cytokine. In this report, sCD23 is shown to sustain the growth of low cell density cultures of a human pre-B-acute lymphocytic leukemia cell line, SMS-SB: no other cytokine tested was able to induce this effect. Flow cytometric analysis indicates that sCD23 acts to prevent apoptosis of SMS-SB cells. SMS-SB cells cultured at low cell density possess low levels of bcl-2 protein. Addition of sCD23 to cells at low cell density maintained bcl-2 expression at levels equivalent to those observed in SMS-SB cells cultured at higher cell densities. No CD23 mRNA was found in SMS-SB cells, ruling out an autocrine function for CD23 in this cell line model. Although SMS-SB cells do not express the known receptors for CD23, namely CD21, CD11b-CD18, or CD11c-CD18, the cells specifically bind CD23-containing liposomes, but not glycophorin-containing liposomes. Binding of CD23-containing liposomes is inhibited by anti-CD23 but not by anti-CD21 or anti-CD11b/c monoclonal antibodies. The data show that sCD23 prevents apoptosis of the SMS-SB cell line by acting through a novel receptor.

L12 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:463188 Document No.: PREV199699185544. Mechanism of T cell subsets and cytokines in the regulation of **IgE** production in exogenous asthma. Wang Danqi, Xia Guoguang (1); Zhao Shulin; et al.. (1) Dep. Respiratory Med., Beijing Ji Shui Tan Hosp., Beijing 100035 China. Zhonghua Weishengwuxue He Mianyixue Zazhi, (1996) Vol. 16, No. 4, pp. 299-301. ISSN: 0254-5101. Language: Chinese. Summary Language: Chinese; English.

AB The peripheral blood of 30 cases of asthma and 30 control adults were measured for T cell subsets with indirect immunofluorescence of monoclonal antibodies, for **IgE**, IL-4 with ELISA, for IL-5 with F123-cell line-biological method, for IL-6 with IL-6-dependent cell line T11 intake method and for CD23 with anti human CD23 McAb. The mechanism of T cells and cytokines in the regulation of **IgE** production in asthma and the effect of cytokines on the pathogenesis of asthma were also studied. The results showed that the levels of **IgE**, IL-4, IL-5, CD23, CD4+ as well as the ratio of CD4/CD8+ in cases of their acute stage were significantly different from those in their remission stage and normal controls P lt .01. In their remission stage, there was no significant **IgE** difference between cases and control P gt 0.05. And there were significant differences of CD4+ CD4/CD8 ratio between cases and normal controls P lt .01. There was no significant difference of CD3, CD4, IL-6 among three groups P gt 0.05. It indicated that the increased production of **IgE** antibody was the key factor in the pathogenesis of exogenous asthma and the cytokines played roles in the process of inflammatory reactions in the airway.

L12 ANSWER 12 OF 17 MEDLINE DUPLICATE 5
 94009242 Document Number: 94009242. PubMed ID: 7691616. CD21 expressed on basophilic cells is involved in histamine release triggered by CD23 and anti-CD21 antibodies. Bacon K; Gauchat J P; Aubry J P; Pechon S; Graber P; Henchoz S; Bonnefoy J Y. Glaxo Institute for Molecular Biology, Plan-Les-Quates, Geneva, Switzerland. EUROPEAN JOURNAL OF IMMUNOLOGY, 1993 Oct; 23 (10): 2721-4. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY; Germany, Federal Republic of. Language: English.

AB Recombinant full-length human CD23 incorporated into fluorescent liposomes was used to detect a ligand for CD23 on the basophilic leukemia cell line, KU 812. Based on our recent finding that CD23 interacts with CD21 on subsets of B and T cells, we investigated if the same ligand was involved on KU 812 cells. An anti-CD21 monoclonal antibody (mAb) BU-33, was able to totally block CD23-liposome binding to KU 812 cells. Moreover, KU 812 cells express CD21 mRNA and have a cell surface molecule that reacts with anti-CD21 mAb. The CD23/CD21 interaction was not merely physical but was also associated with an increase in histamine release by KU 812 cells. Both recombinant soluble CD23 and an anti-CD21 mAb-mediated effect on histamine release was not restricted to and anti-CD21 mAb-mediated effect on histamine release was not restricted to the leukemic cell line, but was also observed with normal human blood basophils. These data demonstrate that CD21 is expressed on basophilic cells and that CD21 controls histamine production upon ligand-induced stimulation (CD23 or anti-CD21 mAb).

L12 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS
 1993:470048 Document No. 119:70048 The mechanisms of IgE uptake by human alveolar macrophages and a human B-lymphoblastoid cell line (Wil-2wt). Richardson, D. R.; Cameron, K.; Robinson, B.; Turner, K. J. (Dep. Microbiol., Univ. West. Australia, Medlands, Australia). Immunology, 79(2), 305-11 (English) 1993. CODEN: IMMUAJ. ISSN: 0019-2805.

AB Human alveolar macrophages (HAM) internalized more IgE (81%) than human Wil-2wt B-lymphoblastoid cells (28%) suggesting a difference in the metabolic processing of the specific IgE receptor (CD23) or, alternatively, the presence of another functionally distinct receptor. The mannose receptor (MR), demonstrated to be present on the AM, may fulfill this role as IgE is heavily mannoseylated and binds to a greater extent to Con A (which has specificity for oligomannose oligosaccharide chains) than other antibody isotypes. The hypothesis of a second IgE receptor was tested using mannan which is a competitive inhibitor of ligand binding to the MR and mannoseylated bovine serum albumin (MBSA) which binds with avidity to the MR. Mannan (0.1 mg/mL) decreased internalized MBSA uptake in the HAM at 37.degree. suggesting the presence of the specific MR. In contrast, Wil-2wt cells did not bind MBSA. Mannan also reduced IgE uptake in the HAM at 37.degree. but had no effect on IgE uptake by Wil-2wt cells. Anti-CD23 monoclonal antibody mAb 135 also partially reduced membrane IgE uptake in HAM while completely inhibiting it by Wil-2wt cells. However, there did not appear to be competition for binding sites between IgE and MBSA in HAM. If only CD23 is involved in IgE uptake by HAM its function appears to be different to that in Wil-2wt cells. Definite involvement of the MR in IgE uptake will require further investigation as it may have an important role in allergic states.

L12 ANSWER 14 OF 17 MEDLINE DUPLICATE 6
 93049152 Document Number: 93049152. PubMed ID: 11955155. Cytokine effects of CD23 are mediated by an epitope distinct from the IgE binding site. Mossalayi M I; Arock M; Telespessio S; Rojstetter H; Bettler B; Gallucci A H; Pflanner E; Jaan F; Leric F; Barfani M. Groupe d'Immunologie-Hematologie Molculaire, CHU Hite-Salpêtrière, Paris, France. EMBO JOURNAL, 1993 Sep 15; 12 (18):4833-8. Journal code: 8236664. ISSN:

- 0261-4189. Pub. country: ENGLAND: United Kingdom. Language: English.
- AB Human CD23 and its soluble forms sCD23 display various biological activities, in addition to their IgE binding function IgE/BF. The IgE binding domain was recently mapped to residues between Cys163 and Cys282 but its involvement in IgE-independent, CD23 functions remains unknown. In order to clarify this point, a series of N-terminal, C-terminal and internal deletion mutants of CD23 or sCD23 were expressed in CHO cells and tested for their ability i. to bind to IgE, ii. to induce colony formation by human myeloid precursor cells, iii. to promote mature T cell marker expression by early prothymocytes, and iv. to regulate IgE synthesis. The present study indicates that cytokine activities require the presence of Cys289, while this amino acid is not necessary for IgE/BF. Blocking experiments using various conformation-sensitive monoclonal antibodies further suggest that active epitope(s) of CD23 in cytokine assays is(are) distinct from those involved in IgE/BF.
- L12 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2002 ACS
1992:253891 Document No. 116:253891 Heterogeneity among Epstein-Barr virus-seropositive donors in the generation of immunoblastic B-cell lymphomas in SCID mice receiving human peripheral blood leukocyte grafts. Picchio, Gaston R.; Kobayashi, Ryo; Kirven, Marybeth; Baird, Stephen M.; Kipps, Thomas J.; Mosier, Donald E. (Div. Immunol., Med. Biol. Inst., La Jolla, CA, 92037, USA). Cancer Res., 52(5), 2466-77 (English) 1992. CODEN: CNREAB. ISSN: 0008-5472.
- AB Epstein-Barr virus (EBV) is assoc. with B-cell malignancy in immunosuppressed humans and SCID mice receiving human peripheral blood leukocyte grafts (hu-PBL-SCID). Here, the process of lymphoma development was further characterized in hu-PBL-SCID mice. EBV-seropos. donors differ markedly in the capacity of their PBL to give rise to immunoblastic lymphomas in SCID mice; some donors (high incidence) generated tumors rapidly in all hu-PBL-SCID mice, other donors (intermediate-low incidence) gave rise to sporadic tumors after a longer latent period (>10 wk), and some donors failed to produce tumors. B-cell lymphomas arising from high incidence donors were monoclonal in origin, and EBV replication was detected in all tumors. Tumors derived from intermediate-low incidence donors were monoclonal or oligoclonal and often had no evidence of viral replication. All tumors, regardless of the donor, resembled EBV-transformed lymphoblastoid cell lines in surface phenotype but differed from lymphoblastoid cell lines by having less Epstein-Barr nuclear antigen 2 and CD23 expression. The variable patterns of lymphomagenesis seen among different EBV-seropos. donors may be explained by lower levels of specific immunity to EBV in high incidence donors, permitting activation of EBV replication and potential transformation of secondary B-cell targets. In addn. there may be differences in the transforming potential of EBV infecting different donors. The use of the hu-PBL-SCID model may help predict patients at high risk for posttransplant or AIDS-assoc. lymphomas.
- L12 ANSWER 16 OF 17 MEDLINE
92364541 Document Number: 92364541. PubMed ID: 1386672. Demonstration of a second ligand for the low affinity receptor for immunoglobulin E (CD23) using recombinant CD23 reconstituted into fluorescent liposomes. Poshon S; Graber P; Yeager M; Jansen K; Bernard A R; Aubry J F; Bennefoy J Y. Glaxo Institute for Molecular Biology, Plan-les-Quates, Geneva, Switzerland. JOURNAL OF EXPERIMENTAL MEDICINE, 1992 Aug 1 176:2 349-57. Journal code: JEMED. ISSN: 0022-0182. Pub. country: United States. Language: English.
- AB Recombinant full-length human CD23 has been incorporated into fluorescent liposomes to demonstrate the existence of a ligand for CD23 that is different from the previously known ligand, immunoglobulin E IgE. The novel ligand for CD23 is expressed

on subsets of normal T cells and B cells as well as on some myeloma cell lines. The interaction of full-length CD23 with its ligand is specifically inhibited by anti-CD23 monoclonal antibodies and by IgE, and it is Ca²⁺ dependent. Moreover, tunicamycin treatment of a CD23-binding cell line, RPMI 8226, significantly reduced the binding of CD23 incorporated into fluorescent liposomes, and a sugar, fucose-1-phosphate, was found to inhibit CD23-liposome binding to RPMI 8226 cells, suggesting the contribution of sugar structures on the CD23 ligand. In addition, CD23-transfected COS cells were shown to form specific conjugates with the cell line RPMI 8226. These data demonstrate that CD23 interacts with a ligand, which is different from IgE, and that CD23 can be considered as a new surface adhesion molecule involved in cell-cell interactions.

L12 ANSWER 17 OF 17 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 8
91341164 EMBASE Document No.: 1991341164. Expression of human recombinant CD23 in insect cells. Jansen K.U.; Shields J.; Gordon J.; Cairns J.; Graber P.; Bonnefoy J.-Y.. Glaxo Institute for Molecular Biology S.A. 46 route des Acacias, 1211 Geneva 24, Switzerland. Journal of Receptor Research 11/1-4 (507-520) 1991.
ISSN: 0197-5110. CODEN: JRRDM. Pub. Country: United States. Language: English. Summary Language: English.

AB Human CD23 (low affinity receptor for IgE) has been expressed in insect cells (Sf9) using the baculovirus expression system and the baculovirus transfer vector pAc373. Insect cells infected with a recombinant baculovirus coding for CD23 synthesized a polypeptide not found in wild-type infected insect cells that had antigenic properties similar to natural CD23 produced in RPMI 8866 cells. Surface expression of recombinant CD23 was demonstrated by its ability to bind IgE. Recombinant CD23 expressed in insect cells had a slightly lower molecular weight (43 kDa) than that of natural CD23 (45 kDa) from RPMI 8866 cells as detected by SDS-PAGE followed by Western-blotting. Affinity-purified recombinant CD23 from infected insect cells showed B-cell growth promoting activity. These observations demonstrate for the first time that biologically active recombinant CD23 can be produced by the baculovirus expression system, thus providing a useful source of recombinant material to elucidate the biological functions of CD23.

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:25:09 ON 24 JUL 2002

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L1      15 S CHIMERIC CD23
L2      6 S L1 AND ANTIBOD?
L3      2 DUP REMOVE L2 4 DUPLICATES REMOVED
L4      1 S HUMANIZED ANTI CD23
L5      22044 S MONOCLONAL
L6      43 S L5 AND HUMAN CD23
L7      7 S L6 AND CHIMERIC
L8      3 DUP REMOVE L7 4 DUPLICATES REMOVED
L9      1 S L5 AND CHIMERIC CD23
L10     0 S L5 AND HUMANIZED CD23
L11     38 S L6 AND IGE
L12     17 DUP REMOVE L11 20 DUPLICATES REMOVED

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=> s l11 and human gamma 1

3 FILES SEARCHED...

L13 11 S L1 AND HUMAN GAMMA 1

=> dup remove l13

PROCESSING COMPLETED FOR L13
L14 3 DUP REMOVE L13 4 DUPLICATES REMOVED

=> d 114 1-3 chib abs

L14 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
0000:320835 Document No.: PREVIEW0000320835. Gamma-1 anti-human
CD23 monoclonal antibodies. Reiff, Mitchell E. ;
Kloetzer, William S.; Nakamura, Takehiko. San Diego, CA, USA. ASSIGNEE:
IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku
Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6911138
January 04, 2000. Official Gazette of the United States Patent and
Trademark Office Patents, (Jan. 4, 2000) Vol. 1230, No. 1, pp. No
pagination. e-file. ISSN: 0098-1133. Language: English.
AB Anti-human **CD23 monoclonal** antibodies
containing human gamma 1 constant domains
and therapeutic uses are provided. These antibodies inhibit IL-4 induced
IgE production by B-cells significantly greater than antibodies
containing other constant domains.

L14 ANSWER 2 OF 3 MEDLINE DUPLICATE 1
2000:150073 Document Number: 20150073. PubMed ID: 10684997. In vitro
IgE inhibition in B cells by anti-CD23 **monoclonal**
antibodies is functionally dependent on the immunoglobulin Fc domain.
Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chant S; Cao X; LaBarre M
Y; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reiff M E.
(Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.)
INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2): 131-41.
Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United
Kingdom. Language: English.
AB CD23, the low affinity receptor for **IgE** (Fc ϵ 2R), is
involved in regulation of **IgE** synthesis by B-lymphocytes. Five
monoclonal antibodies to human **CD23** were
generated from cynomolgus macaques immunized with purified soluble CD23
(sCD23). Four of the five primate antibodies blocked the binding of
IgE complexes to CD23 positive cells and also inhibited the
production of **IgE** in vitro by IL-4 induced human peripheral
blood mononuclear cells (PBMC). The variable domains of several primate
antibodies were utilized to construct chimeric macaque/human
(PRIMATIZED((R))) **monoclonal** antibodies. PRIMATIZED((R)) p5E8G1,
containing human gamma 1 constant region,
inhibited **IgE** production in vitro as efficiently as the parent
primate antibody, but the human gamma 4 constant version, PRIMATIZED((R))
p5E8G4, was not as effective in **IgE** inhibition. An F(ab')₂ of
p5E8G1 did not inhibit **IgE** production but did interfere with
IgE inhibition by the intact anti-CD23 antibody in a dose
dependent fashion. The murine **monoclonal** antibody MHM6
recognizes human **CD23** at a different epitope than
primate antibody 5E8, and inhibits **IgE** production by IL-4
induced PBMC. As with the F(ab')₂ of p5E8G1, the F(ab')₂ of MHM6 also
failed to inhibit **IgE** production. These data imply that the
mechanism by which anti-CD23 antibodies inhibit **IgE** production
requires cross-linking of CD23 to an **IgE** receptor. These data also imply
that neither bivalent cross-linking of CD23 alone or inhibition of CD23
binding to its natural ligands is sufficient to inhibit **IgE**
production.

L14 ANSWER 3 OF 3 CAPLUS COPYRIGHT 1993 ADS
1993:044934 Document No. 1993:044934 Gamma-1 and gamma-3 anti-human
CD23 monoclonal antibodies and use thereof as
therapeutics. Reiff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko
IDEC Pharmaceuticals Corp., USA; Seikagaku Corp., JPN. Int. Appl. WO
93/06661 1993-07-14 14 pp. DESIGNATED STATES: E: AE, AM, AT, AU, AZ,

EA, BB, BG, BF, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GI, GW, HU, ID, IL, IS, JE, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NC, NZ, NL, NO, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, PU, TG, TN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GP, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English)
 CODEN: PIXXD2. APPLICATION: WO 1998-US2553 19980217. PRIORITY: US 1997-803085 19970220.

AB **Monoclonal antibodies which specifically bind human CD23**, the low affinity receptor for **IgE** FcεR1/CD23, and contain either a **human gamma-1** or human gamma-3 const. domain, are disclosed. The antibodies are useful for modulating or inhibiting induced **IgE** expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced **IgE** prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

=> s IgE and allergy
 L15 9 IGE AND ALLERGY
 => s l15 and anti human CD23
 L16 4 FILES SEARCHED...
 L16 0 L15 AND ANTI HUMAN CD23

=> s treatment
 L17 6822620 TREATMENT
 => s l17 and allergy
 L18 28761 L17 AND ALLERGY

=> s l18 and IgE
 L19 4493 L18 AND IGE

=> s l19 and antibody
 L20 2077 L19 AND ANTIBODY

=> s l20 and human CD23
 L21 2 L20 AND HUMAN CD23

=> dup remove l21
 PROCESSING COMPLETED FOR L21
 L22 2 DUP REMOVE L21 (0 DUPLICATES REMOVED)

=> d l22 1-2 chib abs

L22 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2000 ACS
 0001:747174 Document No. 135:287537 Inhibitors for the formation of soluble human CD23 and their use in treatment of diseases. Frey, Juergen Germany. Eur. Pat. Appl. EP 1143910 A1 20011010, 29 pp. DESIGNATED STATES: P: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English)
 CODEN: EFXKXW. APPLICATION: EP 0800-140518 20000407.

AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is described in which the overprod. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. CD23 which inhibitor decreases or blocks selectively the activity of the metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. CD23 is a monoclonal or polyclonal antibody directed against the metalloprotease ADAM9 or wherein the inhibitor is an antisense oligonucleotide which is specific

for c-myc. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medication against inflammatory disorders, autoimmune diseases and allergy.

L22 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
1999:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human
CD23 monoclonal **antibodies** and use thereof as
therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko
Idec Pharmaceuticals Corp., USA; Seikagaku Corp. . PCT Int. Appl. WO
9937099 A1 19990827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH,
GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM; PW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA,
GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English).
CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US
1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind human
CD23, the low affinity receptor for IgE (FcεRII/CD23),
and contain either a human gamma-1 or human gamma-3 const. domain, are
disclosed. The **antibodies** are useful for modulating or
inhibiting induced IgE expression. Accordingly, they have
practical utility in the **treatment** or prophylaxis of disease
conditions wherein inhibition of induced IgE prodn. is
therapeutically desirable, including allergic conditions, autoimmune
diseases and inflammatory diseases.

=> s (reff m7/au or kloetzer w7/au or nakamura t7/au)
L23 42683 (REFF M7/AU OR KLOETZER W7/AU OR NAKAMURA T7/AU)

=> s L23 and CD23 antibody
L24 11 L23 AND CD23 ANTIBODY

=> dup remove L24
PROCESSING COMPLETED FOR L24
L25 3 DUP REMOVE L24 (8 DUPLICATES REMOVED)

=> d L25 1-3 cbib abs

L25 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
200224456 Document Number: 21957817. PubMed ID: 11962725. Anti-CD23
monoclonal antibody inhibits germline Cepsilon transcription in B cells.
Yabuuchi Shingo; Nakamura Takehiko; Kloetzer William S
; Reff Mitchell E. Seikagaku Corporation, Central Research
Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp
Int Immunopharmacol. 2002 Mar 2 4: 453-61. Journal code: 100965259.
ISSN: 1567-5769. Pub. country: Netherlands. Language: English.

AB A chimeric macaque/human PRIMATEZEE anti-CD23 antibody
, p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40
antibody-stimulated IgE production by human peripheral blood mononuclear
cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain
reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline
Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data
suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE
through the inhibition of germline Cepsilon RNA synthesis. Early addition
of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE
inhibition. In contrast, later addition of p6G5G1 still showed inhibition
of increased levels of surface CD23, which is normally upregulated by
stimulation with IL-4 and anti-CD40.

- 125 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
 2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena P A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY. (2000 Feb) 22 (2), 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.
- AB CD23, the low affinity receptor for IgE Fc ϵ 2, is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED(R)) monoclonal antibodies. PRIMATIZED(R) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED(R) p5E8G4, was not as effective in IgE inhibition. An F(ab') (2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab') (2) of p5E8G1, the F(ab') (2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-CD23 antibodies inhibit IgE production requires cross-linking of CD23 to an IgE receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.
- L25 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
 1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. Reff, Mitchell R.; Barnett, Richard Spence; McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US 5998144 A. 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.
- AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predet. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, rat hamster kidney cells, COS cells, HEK cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors. Molly and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, M-Neomycin

phosphotransferase exon1, N2-Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and polyoma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human CD23 antibody and immunoadhesin in Desmond marked CHO cells was achieved.

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NEWS 5	Apr 19	US Patent Applications available in IFICIS, IPIPAT, and IFIUSB
NEWS 6	Apr 22	Records from IF.com available in CASPLUS, BIOPLUS, and COAPLUS
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NEWS 8	Apr 22	Federal Research in Progress FELIP now available
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NEWS 10	Jun 18	NEILINE Reload
NEWS 11	Jun 18	EXTFULL has been reloaded
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NEWS 13	Jul 22	USAN to be reloaded July 29, 2002

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PASSWORD:

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NEWS 4 Feb 01 DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6 Mar 08 Gene Names now available in BIOSIS
NEWS 7 Mar 22 TOXLIT no longer available
NEWS 8 Mar 22 TRCTHERMO no longer available
NEWS 9 Mar 28 US Provisional Priorities searched with P in CA/CAPLUS and USPATFULL
NEWS 10 Mar 28 LIPINSKI/CALC added for property searching in REGISTRY
NEWS 11 Apr 02 PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 12 Apr 08 "Ask CAS" for self-help around the clock
NEWS 13 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area
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NEWS 16 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 19 Jun 03 New e-mail delivery for search results now available
NEWS 20 Jun 10 MEDLINE Reload
NEWS 21 Jun 10 PCTFULL has been reloaded
NEWS 22 Jul 02 FOREGE no longer contains STANDARDS file segment

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AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002

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ENTRY	SESSION
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=> s method

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L1 10122901 METHOD

=> s l1 adn inhibit IgE

MISSING OPERATOR L1 ADN

The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l1 and inhibit IgE

L2 150 L1 AND INHIBIT IGE

=> s l2 and "anti human CD23"

L3 0 L2 AND "ANTI HUMAN CD23"

=> s chimeric human CD23

L4 1 CHIMERIC HUMAN CD23

=> d l4 cbib abs

L4 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

2002:370946 Document No.: PREV200200370946. Antibodies against the stalk region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis. Caven, Timothy Hays; Ma, Check; Beavil, Rebecca; Beavil, Andrew; Ghitlano, Rodolpho; Gould, Hannah; Conrad, Daniel. (1) Virginia Commonwealth University, 1017 East Marshall Street, Richmond, VA, 23298 USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1239. <http://www.fasebj.org/>. print. Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0890-6638. Language: English.

AB The stalk region of human CD23 comprising a.a. 48-183 was expressed in E. coli and purified. In addition a **chimeric human CD23** was prepared consisting of the extracellular region of CD23 linked to a modified leucine zipper L2-CD23. Polyclonal antisera were produced in rabbits and shown to block binding of IgE to CD23 both on cell surfaces as well as the interaction of L2-CD23 with IgE in an ELISA based assay. The antisera was also shown to inhibit IgE synthesis in an anti-CD4/IL-4 stimulated human PBEL model. The inhibition was dose dependent and essentially complete blockage of IgE production was seen at a relatively low dose of anti-stalk. FACS analysis using CD23+5

lymphoblastoid cells indicated little if any endocytosis and/or protection from cleavage induced by the anti-stalk. Monoclonal antibodies against the human stalk have also been prepared and these are being analyzed for the capacity to inhibit IgE binding and IgE synthesis, as well as compare their efficacy to the anti-lectin mabs. The results indicate that targeting the stalk region is efficacious with respect to blocking IgE production.

=> s 12 and CD23 antibody
L5 0 L2 AND CD23 ANTIBODY

=> s antibody?
L6 2321935 ANTIBOD?

=> s 16 and CD23
L7 3178 L6 AND CD23

=> s 17 and humanized
L8 16 L7 AND HUMANIZED

=> s 18 and primate
L9 1 L8 AND PRIMATE

=> d 19 chib abs

L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human

CD23 monoclonal antibodies and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PFXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind human **CD23**, the low affinity receptor for IgE (FcεRII/**CD23**), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

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PROCESSING COMPLETED FOR L8
L10 12 DUF REMOVE L8 4 DUPLICATES REMOVED

=> d 110 1-12 chib abs

L11 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
2003:000424 Document No. 116:246118 Combination therapy for treatment of autoimmune diseases using B cell depleting immunoregulatory **antibody** combination... Hanna, Mabil Idec Pharmaceuticals, USA . PCT Int. Appl. WO 2001001112 A2 20010201, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, BA, BE, BG, BF, BY, CA, CH, CI, CO, CU, CZ, DE, EE, ES, FI, GB, GE, GM, GU, IL, IN, JP, KE, KR, KZ, LC, LR, LU, MW, MX, NC,

HZ, PL, PT, RO, RU; PW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English).
 CODEN: PIXXDD. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US
 2000-PV257147 20001222.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

110 ANSWER 2 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 2002036168 EMBASE Anti-IgE-**antibodies** in the treatment of allergic diseases. Soler M., M. Soler, Pulmonary Division, University Hospital, CH-4031 Basel, Switzerland. msoler@uhbs.ch. Revue Francaise d'Allergologie et d'Immunologie Clinique 42/1 (45-49) 2002.
 Refs: 25.
 ISSN: 0335-7457. CODEN: RFAIBB. Pub. Country: France. Language: English. Summary Language: English; French.

AB In an established type-I allergy, the IgE molecule is the main mechanism by which the organism specifically recognizes the inhaled allergen. When the IgE molecule is bound to its high-affinity receptor on the surface of a mast cell, it also provides the link between the allergen and the immediate mast cell activation and mediator release, which are the central steps in the type-I immune response. The **humanized monoclonal Anti-IgE antibody** omalizumab binds to free IgE molecules in the serum and thereby prevents them from attaching to the high affinity IgE-receptors on the mast cell surface. This treatment, when given on a regular basis, is able to block the antigen-induced tissue responses in the bronchi and in the skin. In large scale clinical trials it proved to be effective in controlling allergic asthma, preventing exacerbations and reducing the need for inhaled and/or systemic steroid treatment. In more than 1500 patients treated for at least 1 year, the compound showed excellent safety and tolerability. This new treatment may have an important place in the future treatment of moderate to severe allergic asthma, especially if the patient needs a complex treatment that still allows for recurrent exacerbations. A major advantage of this treatment lies in its ability to control nasal and eye symptoms of the allergic disease at the same time. .COPYRGT. 2002 Editions scientifiques et medicales Elsevier SAS.

110 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
 2001:747174 Document No. 135:287537 Inhibitors for the formation of soluble human **CD23** and their use in treatment of diseases. Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp.
 DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXNWD.
 APPLICATION: EP 2000-107515 20000407.

AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is described in which the overprod. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. **CD23** which inhibitor decreases or blocks selectively the activity of the metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. **CD23** is a monoclonal or polyclonal **antibody** directed against the metalloprotease ADAM9 or wherein the inhibitor is an antisense oligonucleotide which is specific for s-mys. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and allergy.

2001562398 Document Number: 21203341. PubMed ID: 11307028.

Humanized anti-IgE mAb Hu-901 prevents the activation of allergen-specific T cells. van Neeven R J; van Roemen C P; Thomas W R; de Boer M; Knol E F; Davis F M. *Tanox Pharma BV, Amsterdam, The Netherlands.. jostvanneerven@tanox.nl*. INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, 2001 Jan-Mar; 124 (1-3): 490-2. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: As a result of the very efficient capture of allergens by IgE that focuses to **CD23** on B cells or FcεpsilonR1 on dendritic cells, allergen-specific T cells can be activated after exposure to very low levels of allergens. This IgE-mediated allergen presentation is 100- to 1,000-fold more efficient than fluid phase endocytosis. The aim of the present study was to determine whether **humanized anti-IgE mAb Hu-901** can prevent the activation of allergen-specific T cells by inhibiting IgE-mediated allergen presentation. METHODS: A house dust mite major allergen Der p 1-specific T cell line was generated from an allergic asthma patient, and a model was set up to show IgE-facilitated allergen presentation via **CD23** on EBV-transformed B cells. In addition, experiments were performed by FACS analysis, detecting the presence of IgE-allergen complexes bound to EBV-B cells by polyclonal FITC-labeled anti-IgE antisera. RESULTS: The anti-IgE mAb Hu-901 inhibited proliferation of allergen-specific T cells at low allergen concentrations. Inhibition was dose-dependent. This effect could be explained by Hu-901 inhibition of binding of allergen-IgE complexes to **CD23** expressed on EBV-transformed B lymphocytes. CONCLUSIONS: These data clearly indicate that anti-IgE **antibodies** for the treatment of allergy exert their effect not only by inhibiting mast cell/basophil degranulation, but also by preventing T cell activation, which possibly explains the effect of anti-IgE treatment on late-phase reactions noted in clinical studies.

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L10 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS

2001:361001 Document No. 136:52380 Allergen, IgE and mast-cell-directed therapies: An overview. Larche, Mark; Kay, A. Barry (Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College School of Medicine, London, UK). Progress in Respiratory Research, 31(New Drugs for Asthma, Allergy and COPD), 182-185 (English); 2001. CODEN: PRRRAE. ISSN: 1422-2140. Publisher: S. Karger AG.

AB A review. In addn. to traditional drug development strategies, a no. of current approaches focus on modulation of the immune response to allergens or the allergens themselves. Disease-modulating specific immunotherapy has been used for many years and has been shown to be efficacious, although this form of treatment is slow and carries the risk of systemic adverse reactions. The identification of naturally occurring allergen isoforms of the native protein which do not bind IgE has led to modification of a no. of allergens by site-directed mutagenesis. Such proteins have a reduced or absent interaction with IgE while retaining much of their ability to stimulate T cells. The improved safety profile of such mols. may result in larger, more efficacious doses of protein being given with improved safety. Fragments of allergen mols., such as peptides, are also under development, employing a similar rationale of destroying IgE binding epitopes while retaining T cell determinants. Neutralization of specific mols. in the inflammatory cascade is currently being addressed with "**humanized**" monoclonal **antibodies** and sol. receptors/receptor antagonists, directed towards IgE, cytokines such as IL-4 and IL-5, and cell surface mols. such as **CD23**.

L11 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS

2001:366119 Document No. 134:16552 Treating allergic diseases with immunotherapy and IgE antagonists. Larche, Mark; van Neeven, Jost; Tanox, Inc., USA. J. Exp. Med. 193:1655-1665 (2001) 16 pp. DESIGNATED STATES: W1, AL, AR, AZ, CA, BA, BB, BG, BR, BY, CA, CN, CU, CZ,

EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MM, MW, MX, NO, NZ, PL, PO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US13446 20000516. PRIORITY: US 1999-PV136068 19990526.

AB The invention relates to methods of treating allergic diseases with a combination of immunotherapy and IgE antagonists by inhibiting the binding of IgE mols. to IgE receptors. Uge Fc receptor type I and **CD23**, expressed by cells of the immune system. In one embodiment, anti-IgE **antibodies** are used and allergy inhibitors. Disclosed is a mouse (TES-C21) and chimeric mouse-human (TESC-2) anti-IgE **antibody** and fragments as allergy inhibitors.

L10 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS
2000:457197 Document No. 133:57697 Enhanced proteins production in cell

culture stimulated by unusually low alkanolic acid concentrations. Islam, Seema; Sharp, Nigel Alan (Glaxo Group Limited, UK). PCT Int. Appl. WO 2000039282 A1 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP10157 19991221. PRIORITY: GB 1998-28624 19981223.

AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkanolic acid or its salt at a maintained concn. of less than 0.1mM. Thus, NSO cells transfected with an IgG1 humanized anti-**CD23** antibody was cultured for 56 days in a draw and fill repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in **antibody** prodn. over the control.

L10 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS
1999:736930 Document No. 131:350265 **Antibodies to CD23.**

Bonnefof, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc epsilon RII) receptor antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of $1.5-1.85 \times 10^6$ M⁻¹ s⁻¹ and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L10 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS
1999:604934 Document No. 133:215703 Gamma-1 and gamma-3 anti-human

CD23 monoclonal **antibodies** and use thereof as therapeutics. Reiff, Mitchell E.; Kibetzer, William S.; Nakamura, Takehiko

Pharmaceuticals Corp., USA; Seikagaku Corp. . PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BP, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

- AB Monoclonal antibodies which specifically bind human **CD23**, the low affinity receptor for IgE FcεRII/CD23, and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The antibodies are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L10 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380154 Document No. 125:56235 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Leconet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

- AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal antibodies decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L10 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul Glaxo Group Limited, UK. PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

- AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** antibody, **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal antibodies decrease **CD23**-liposome binding to activated blood monocytes, increases of

monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L10 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS
1995-799548 Document No. 123:196599 IgE antagonists for treatment of parasitic infection. Amiri, Payman; Haak-Fredrichs, Mary; Jardieu, Paula M. Genentech, Inc., USA. PCT Int. Appl. WO 95/1981 A1 19950720, 28 pp. DESIGNATED STATES: W: JP, MX; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TE, TG. English. CODEN: PIMXD2. APPLICATION: WO 1995-0587 19950108. PRIORITY: US 1994-184083 19940118.
A5 This invention concerns a method for the prevention and treatment of parasitic infection by administering an IgE antagonist. The invention further concerns pharmaceutical compns. and bispecific mols. useful in such method. In example, anti-IgE monoclonal **antibody** reduced serum IgE, serum interleukin 4 and interferon .gamma., number of adult worms and eggs, and hepatosplenomegaly following Schistosoma mansoni infection in mice. The IgE antagonist also reduced the enhancement of **CD23** expression in splenic lymphoid cells.

=> s monkey anti human CD23
L11 0 MONKEY ANTI HUMAN CD23

=> d his

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 13:19:38 ON 05 JUL 2002

L1 10122901 S METHOD
L2 150 S L1 AND INHIBIT IGE
L3 0 S L2 AND "ANTI HUMAN CD23"
L4 1 S CHIMERIC HUMAN CD23
L5 0 S L2 AND CD23 ANTIBODY
L6 2321935 S ANTIBOD?
L7 3178 S L6 AND CD23
L8 16 S L7 AND HUMANIZED
L9 1 S L8 AND PRIMATE
L10 12 DUP REMOVE L8 (4 DUPLICATES REMOVED)
L11 0 S MONKEY ANTI HUMAN CD23

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4 FILES SEARCHED...
L12 5 L7 AND HUMAN GAMMA 1 CONSTANT REGION

=> dup remove l12
PROCESSING COMPLETED FOR L12
L13 1 DUP REMOVE L12 (4 DUPLICATES REMOVED)

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L13 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
2000150073 Document Number: 20150073. PubMed ID: 1084997. In vitro IgE inhibition in B cells by anti-**CD23** monoclonal **antibodies** is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brans P; Hariharan K; Shamati S; Jao X; LaBarre M C; Chinn P C; Morena P A; Shostowsky W S; Li Y P; Chen A; Peiff M E. Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan. INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 2001 Feb 22; 23: 131-41. Journal code: 7914799. ISSN: 0192-5541. Pub. country: ENGLAND; United Kingdom. Language: English.
A5 **CD23**, the low affinity receptor for IgE Fc-gammaR1, is

involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal **antibodies** to human **CD23** were generated from cynomolgus macaques immunized with purified soluble **CD23** (sCD23). Four of the five primate **antibodies** blocked the binding of IgE complexes to **CD23** positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate **antibodies** were utilized to construct chimeric macaque/human (PRIMATIZED(R)) monoclonal **antibodies**. PRIMATIZED(R) p5E8G1, containing human **gamma 1 constant region**, inhibited IgE production in vitro as efficiently as the parent primate **antibody**, but the human gamma 4 constant version, PRIMATIZED(R) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23 antibody** in a dose dependent fashion. The murine monoclonal **antibody** MHM6 recognizes human **CD23** at a different epitope than primate **antibody** 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23 antibodies** inhibit IgE production requires cross-linking of **CD23** to an IgG receptor. These data also imply that neither bivalent cross-linking of **CD23** alone or inhibition of **CD23** binding to its natural ligands is sufficient to inhibit IgE production.

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=> s primatized CD23
L14          0 PRIMATIZED CD23

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 13:19:38 ON
05 JUL 2002
L1      10122901 S METHOD
L2          150 S L1 AND INHIBIT IGE
L3          0 S L2 AND "ANTI HUMAN CD23"
L4          1 S CHIMERIC HUMAN CD23
L5          0 S L2 AND CD23 ANTIBODY
L6      2321935 S ANTIBOD?
L7          3178 S L6 AND CD23
L8          16 S L7 AND HUMANIZED
L9          1 S L8 AND PRIMATE
L10         12 DUP REMOVE L8 (4 DUPLICATES REMOVED)
L11          0 S MONKEY ANTI HUMAN CD23
L12          5 S L7 AND HUMAN GAMMA 1 CONSTANT REGION
L13          1 DUP REMOVE L12 (4 DUPLICATES REMOVED)
L14          0 S PRIMATIZED CD23

=> s 17 and human IgG1 Fc
L15          3 L7 AND HUMAN IGG1 FC

=> dup remove l15
PROCESSING COMPLETED FOR L15
L16          1 DUP REMOVE L15 (3 DUPLICATES REMOVED)

=> d l16 thib aks

L16 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
023055(1) Document Number: 023055(2). PubMed ID: 1878075. Soluble forms of
CD23 inhibit biologic responses of human B cells. Fanslow W C; Anderson D
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M; Grabstein K H; Clark E A; Cosman D; Armitage R J. Department of Immunology, Immunex Research and Development Corporation, Seattle, WA 98161. JOURNAL OF IMMUNOLOGY, 1992 Jul 15; 149 (2): 655-60. Journal code: 2385117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We have expressed the CD40 surface Ag as both a soluble 28-kDa molecule and a 57-kDa Fc fusion protein containing the **human IgG1 Fc** region. Soluble CD40 and the Fc fusion protein inhibited the proliferative response of anti-IgM-activated human B cells to the CD40 mAb G28-5. Similarly, G28-5- and IL-4-induced IgE secretion from PBMC depleted of T cells was effectively blocked by both forms of soluble CD40. Although the soluble constructs of CD40 had only a minimal inhibitory effect on IL-4-mediated proliferation of anti-IgM-activated B cells, IL-4-induced soluble **CD23** shedding from both PBMC and T cells depleted of PBMC, and IgE secretion from PBMC, were significantly reduced in a concentration-dependent manner when soluble CD40 was present in the culture. The data presented demonstrate that both soluble forms of the CD40 molecule are biologically active, and suggest that the ligand for CD40 is inducible in IL-4-stimulated cultures and that it mediates both shedding of sCD23 and IgE secretion.

=> s l7 and humanized
L17 16 L7 AND HUMANIZED

=> dup remove l17
PROCESSING COMPLETED FOR L17
L18 12 DUP REMOVE L17 (4 DUPLICATES REMOVED)

=> d l18 l-12 cbib abs

L18 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
2002:220424 Document No. 136:246408 Combination therapy for treatment of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CL, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L18 ANSWER 2 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2002036168 EMBASE Anti-IgE-**antibodies** in the treatment of allergic diseases. Soler M. M. Soler, Pulmonary Division, University Hospital, CH-4031 Basel, Switzerland. msoler@uhbs.ch. Revue Francaise d'Allergologie et d'Immunologie Clinique 42/1 45-49 2002.
Refs: 25.
ISSN: 0335-7457. CODEN: RFAIBB. Pub. Country: France. Language: English. Summary Language: English; French.

AB In an established type-I allergy, the IgE molecule is the main mechanism by which the organism specifically recognizes the inhaled allergen. When the IgE molecule is bound to its high-affinity receptor on the surface of a mast cell, it also provides the link between the allergen and the immediate mast cell activation and mediator release, which are the central steps in the type-I immune response. The **humanized** monoclonal

Anti-IgE **antibody** omalizumab binds to free IgE molecules in the serum and thereby prevents them from attaching to the high affinity IgE-receptors on the mast cell surface. This treatment, when given on a regular basis, is able to block the antigen-induced tissue responses in the bronchi and in the skin. In large scale clinical trials it proved to be effective in controlling allergic asthma, preventing exacerbations and reducing the need for inhaled and/or systemic steroid treatment. In more than 1500 patients treated for at least 1 year, the compound showed excellent safety and tolerability. This new treatment may have an important place in the future treatment of moderate to severe allergic asthma, especially if the patient needs a complex treatment that still allows for recurrent exacerbations. A major advantage of this treatment lies in its ability to control nasal and eye symptoms of the allergic disease at the same time. .COPYRGT. 2002 Editions scientifiques et medicales Elsevier SAS.

L18 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS

2001:747174 Document No. 135:287537 Inhibitors for the formation of soluble human **CD23** and their use in treatment of diseases. Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2000-107515 20000407.

AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is described in which the overprod. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. **CD23** which inhibitor decreases or blocks selectively the activity of the metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. **CD23** is a monoclonal or polyclonal **antibody** directed against the metalloprotease ADAM9 or wherein the inhibitor is an antisense oligonucleotide which is specific for c-myc. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and allergy.

L18 ANSWER 4 OF 12 MEDLINE DUPLICATE 1
2001262398 Document Number: 21203341. PubMed ID: 11307028.

Humanized anti-IgE mAb Hu-901 prevents the activation of allergen-specific T cells. van Neerven R J; van Roomen C P; Thomas W R; de Boer M; Knol E F; Davis F M. (Tanox Pharma BV, Amsterdam, The Netherlands.. joostvanneerven@tanox.nl). INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Jan-Mar) 124 (1-3) 400-2. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English. AB BACKGROUND: As a result of the very efficient capture of allergens by IgE that focuses to **CD23** on B cells or FcεpsilonR1 on dendritic cells, allergen-specific T cells can be activated after exposure to very low levels of allergens. This IgE-mediated allergen presentation is 100- to 1,000-fold more efficient than fluid phase endocytosis. The aim of the present study was to determine whether **humanized anti-IgE mAb Hu-901** can prevent the activation of allergen-specific T cells by inhibiting IgE-mediated allergen presentation. METHODS: A house dust mite major allergen Der p 1-specific T cell line was generated from an allergic asthma patient, and a model was set up to show IgE-facilitated allergen presentation via **CD23** on EBV-transformed B cells. In addition, experiments were performed by FACS analysis, detecting the presence of IgE-allergen complexes bound to EBV-B cells by polyclonal FITC-labeled anti-IgE antisera. RESULTS: The anti-IgE mAb Hu-901 inhibited proliferation of allergen-specific T cells at low allergen concentrations. Inhibition was dose-dependent. This effect could be explained by Hu-901 inhibition of binding of allergen-IgE complexes to **CD23** expressed on EBV-transformed B lymphocytes. CONCLUSIONS: These data

clearly indicate that anti-IgE **antibodies** for the treatment of allergy exert their effect not only by inhibiting mast cell/basophil degranulation, but also by preventing T cell activation, which possibly explains the effect of anti-IgE treatment on late-phase reactions noted in clinical studies.

Copyright 2001 S. Karger AG, Basel

L18 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS

2001:361901 Document No. 136:52360 Allergen, IgE and mast-cell-directed therapies: An overview. Larche, Mark; Kay, A. Barry (Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College School of Medicine, London, UK). Progress in Respiratory Research, 31/New Drugs for Asthma, Allergy and COPD, 182-185 (English) 2001. CODEN: PRRAAE. ISSN: 1422-2140. Publisher: S. Karger AG.

AB A review. In addn. to traditional drug development strategies, a no. of current approaches focus on modulation of the immune response to allergens or the allergens themselves. Disease-modulating specific immunotherapy has been used for many years and has been shown to be efficacious, although this form of treatment is slow and carries the risk of systemic adverse reactions. The identification of naturally occurring allergen isoforms of the native protein which do not bind IgE has led to modification of a no. of allergens by site-directed mutagenesis. Such proteins have a reduced or absent interaction with IgE while retaining much of their ability to stimulate T cells. The improved safety profile of such mols. may result in larger, more efficacious doses of protein being given with improved safety. Fragments of allergen mols., such as peptides, are also under development, employing a similar rationale of destroying IgE binding epitopes while retaining T cell determinants. Neutralization of specific mols. in the inflammatory cascade is currently being addressed with "humanized" monoclonal **antibodies** and sol. receptors/receptor antagonists, directed towards IgE, cytokines such as IL-4 and IL-5, and cell surface mols. such as **CD23**.

L18 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS

2000:861519 Document No. 134:16552 Treating allergic diseases with immunotherapy and IgE antagonists. Deboer, Mark; Van Neerven, Joost (Tanox, Inc., USA). PCT Int. Appl. WO 2000/072879 A1 20001207, 31 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US13446 20000516. PRIORITY: US 1999-PV136068 19990526.

AB The invention relates to methods of treating allergic diseases with a combination of immunotherapy and IgE antagonists by inhibiting the binding of IgE mols. to IgE receptors (IgE Fc receptor type I and **CD23**), expressed by cells of the immune system. In one embodiment, anti-IgE **antibodies** are used and allergy inhibitors. Disclosed is a mouse (TES-C21) and chimeric mouse-human TES-C21 anti-IgE **antibody** and fragments as allergy inhibitors.

L18 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS

2000:467197 Document No. 133:57667 Enhanced proteins production in cell culture stimulated by unusually low alkaloids acid concentrations. Islam, Seema; Sharp, Nigel Alan. Glaxo Group Limited, UK. PCT Int. Appl. WO 2000/03202 A1 20000706, 31 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BE, BG, BF, BY, CA, CH, CN, CR, CU, CZ, DE, EE, ES, FI, GE, GR, GH, GM, HP, HU, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MC, MG, MK, MN, MW, MX, NC, NE, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AL, BY, BG, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG.

CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SI, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP10157 19991221. PRIORITY: GB 1998-28624 19981223.

AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkanolic acid or its salt at a maintained concn. of less than 0.1mM. Thus, NSO cells transfected with an IgG1 **humanized anti-CD23 antibody** was cultured for 56 days in a draw and fill repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in **antibody** prodn. over the control.

L18 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS
1999:736930 Document No. 131:350265 **Antibodies to CD23.**
Bonney, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, UG, US, UZ, VN, YU, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and **humanized antibodies** which bind to the **CD23** (Fc ϵ 1RII receptor) antigen. In one example, **humanized IgG1**, with mutations to eliminate Clq and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 10⁶ M⁻¹ s⁻¹ and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L18 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human **CD23 monoclonal antibodies** and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idex Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind human **CD23**, the low affinity receptor for IgE (Fc ϵ 1RII/CD23), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L18 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS
1998:330154 Document No. 125:86236 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonney, Jean-Yves Marcel Paul; Lecanet-Hersches, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9812742 A1 19980502, 81 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CI, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE,

- KG, KP, KR, KZ, LK, LF, LT, LU, LV, MD, MG, MK, MI, MW, MX, NO, NZ, PL, PT, PQ, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
- AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 kDa protein expressed on endothelial cells or a 115 kDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.
- L18 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS
1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LF, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
- AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** **antibody**, **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.
- L18 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS
1995:789548 Document No. 123:196599 IgE antagonists for treatment of parasitic infection. Amiri, Payman; Haak-Fredsch, Mary; Jardieu, Paula M. (Genentech, Inc., USA). PCT Int. Appl. WO 9519181 A1 19950720, 28 pp. DESIGNATED STATES: W: JP, MX; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: US 1995-US87 19950105. PRIORITY: US 1994-184083 19940116.
- AB This invention concerns a method for the prevention and treatment of parasitic infection by administering an IgE antagonist. The invention further concerns pharmaceutical compns. and bispecific mols. useful in such method. In example, anti-IgE monoclonal **antibody** reduced serum IgE, serum interleukin 4 and interferon .gamma., number of adult worms and eggs, and hepatosplenomegaly following *Schistosoma mansoni* infection in mice. The IgE antagonist also reduced the enhancement of **CD23** expression in splenic lymphoid cells.

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=> s anti human CD23
L18          s ANTI HUMAN CD23
=> dup remove l18
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PROCESSING COMPLETED FOR L19
L20 5 DUP REMOVE L19 *3 DUPLICATES REMOVED

=> d 120 1-5 cblb abs

L20 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:320835 Document No.: PREV200000320835. Gamma-1 anti-
human CD23 monoclonal antibodies. Reff, Mitchell E. 1;
Kloetzer, William S.; Nakamura, Takehiko. 1, San Diego, CA USA. ASSIGNEE:
IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku
Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6011138
January 04, 2000. Official Gazette of the United States Patent and
Trademark Office Patents, (Jan. 4, 2000) Vol. 1230, No. 1, pp. No
pagination. e-file. ISSN: 0098-1133. Language: English.

AB Anti-human CD23 monoclonal antibodies
containing human gamma 1 constant domains and therapeutic uses are
provided. These antibodies inhibit IL-4 induced IgE production by B-cells
significantly greater than antibodies containing other constant domains.

L20 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
1999:779157 Document No. 132:19632 Method for integrating genes at specific
sites in mammalian cells via homologous recombination and vectors for
accomplishing the same. Reff, Mitchell R.; Barnett, Richard Spence;
McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US
5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English).
CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US
1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a
target site in a mammalian cell via homologous recombination is described.
This method provides for the reproducible selection of cell lines wherein
a desired DNA is integrated at a predetd. transcriptionally active site
previously marked with a marker plasmid (Desmond). This unique site may
be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker
plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase
exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40
enhancers, splice acceptor site, mouse beta globin major promoter, bovine
growth hormone polyadenylation site, SV40 early and late polyadenylation
sites. The selectable marker proteins may include neomycin
phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase,
hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase,
glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase.
Marked CHO cells were produced and characterized. Other cells that may be
marked include myeloma cells, baby hamster kidney cells, COS cells, NSO
cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable
for the prodn. of mammalian cell lines which secrete mammalian proteins at
high levels, in particular Igs. Novel targeting vectors Molly and
vector combinations for use in the subject cloning method are also
provided. This Molly vector contains dihydrofolatereductase, NI+Neomycin
phosphotransferase exon1, NI+Neomycin phosphotransferase exon 2, anti-CD20
light chain leader-variable, human kappa const., anti-CD20 heavy chain
leader-variable, human gamma 1 const., Salmonella histidinol
dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor,
CMV promoter/enhancer, HSV TK promoter and polyoma enhancer, mouse beta
globin major promoter, SV40 late polyadenylation, bovine growth hormone
polyadenylation. Expression of an Anti-CD20 and Anti-
human CD23 antibody and immunoadhesin in Desmond marked
CHO cells was achieved.

L20 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
1999:64904 Document No. 139:115703 Gamma-1 and gamma-2 anti-
human CD23 monoclonal antibodies and use thereof as
therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko
Idec Pharmaceuticals Corp., USA; Seikagaku Corp. . PCT Int. Appl. WO

9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English).
CODEN: RIXMD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal antibodies which specifically bind human CD23, the low affinity receptor for IgE (FcεRII/CD23), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The antibodies are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L20 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:463188 Document No.: PREV199699185544. Mechanism of T cell subsets and cytokines in the regulation of IgE production in exogenous asthma. Wang Danqi, Xia Guoguang (1); Zhao Shulin; et al.. (1) Dep. Respiratory Med., Beijing Ji Shui Tan Hosp., Beijing 100035 China. Zhonghua Weishengwuxue He Mianyixue Zazhi, (1996) Vol. 16, No. 4, pp. 299-301. ISSN: 0254-5101. Language: Chinese. Summary Language: Chinese; English.

AB The peripheral blood of 30 cases of asthma and 30 control adults were measured for T cell subsets with indirect immunofluorescence of monoclonal antibodies, for IgE, IL-4 with ELISA, for IL-2 with T-cell line-biological method, for IL-6 with IL-6-dependent cell line 7TD1 intake method and for CD23 with anti human CD23 McAb. The mechanism of T cells and cytokines in the regulation of IgE production in asthma and the effect of cytokines on the pathogenesis of asthma were also studied. The results showed that the levels of IgE, IL-4, IL-2, CD23, CD8+ as well as the ratio of CD4/CD8+ in cases of their acute stage were significantly different from those in their remission stage and normal controls (P lt 0.01). In their remission stage, there was no significant IgE difference between cases and control (P gt 0.05). And there were significant differences of CD8+ CD4/CD8 ratio between cases and normal controls (P lt 0.01). There was no significant difference of CD3, CD4, IL-6 among three groups (P gt 0.05). It indicated that the increased production of IgE antibody was the key factor in the pathogenesis of exogenous asthma and the cytokines played roles in the process of inflammatory reactions in the airway.

L20 ANSWER 5 OF 5 MEDLINE DUPLICATE 1
91010830 Document Number: 91010830. PubMed ID: 1698879. A bioassay for the measurement of human interleukin-4. Siegel J P; Mostowski H S. (Division of Cytokine Biology, Center for Biologics Evaluation and Research, FDA, Bethesda, MD.) JOURNAL OF IMMUNOLOGICAL METHODS, (1990 Sep 14) 132 (2) 287-95. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB We have developed a bioassay for human IL-4 based upon its ability to upregulate CD23 low affinity IgE receptor expression. Ramos, a B lymphocyte line derived from a Burkitt lymphoma, was repetitively subcloned yielding a clone, Ramos.G6.C13, which is several fold more sensitive to this effect of IL-4. In microtiter plates cells were cultured for 48 h in the presence of dilutions of recombinant human IL-4 or samples, and then stained with murine anti-human CD23 and goat anti-mouse IgG-FITC. IL-4 induced an eight-fold increase of channel shift in fluorescence intensity as measured by flow cytometry. Significant effects were observed at an IL-4 concentration of 5-100 pg/ml and increased with concentrations up to 500 pg/ml. Inter- and intra-assay coefficients of variation were 10- and 11- respectively. The

bioassay showed good specificity for IL-4; however, tumor necrosis factors alpha and beta, at optimal concentrations, gave readings barely at the threshold of detection.

=> s 'rempef f7/au or brooks k7/au
L21 1255 (REMPEF F7/AU OR BROOKS K7/AU)

=> s l21 and anti CD23
L22 0 L21 AND ANTI CD23

=> s l21 and antibody
L23 63 L21 AND ANTIBODY

=> s l23 and CD23
L24 0 L23 AND CD23

=> s l23 and IgE
L25 1 L23 AND IGE

=> d l25 cbib abs

L25 ANSWER 1 OF 1 MEDLINE
95048595 Document Number: 95048595. PubMed ID: 7525472. B-1 cells in systemic autoimmune responses: IgM+, Fc epsilon Rdu11 B cells are lost during chronic graft-versus-host disease but not in murine AIDS or collagen-induced arthritis. Iciek L A; Waldschmidt T J; Griffiths M M; **Brooks K H.** (Department of Microbiology, Michigan State University, East Lansing 48824.) IMMUNOLOGICAL INVESTIGATIONS, (1994 Aug) 23 (4-5) 293-311. Journal code: 8504629. ISSN: 0882-0139. Pub. country: United States. Language: English.

AB The potential role of B-1 cells (i.e. the CD5+ B cell and "sister" B cell subsets) in autoimmunity is controversial. CD5+ B cells have been shown to secrete **antibodies** of similar specificity as those found in many systemic autoimmune diseases; in addition, increases in CD5+ B cell frequency have been reported in patients suffering from rheumatoid arthritis, Sjogren's syndrome, myasthenia gravis, insulin-dependent diabetes mellitus and Hashimoto's thyroiditis. Whether these increases are due to expansion of B-1 lineage cells in the human or due to activation-induced expression of CD5 by conventional B cells is unclear. In the present study, we used three murine models of systemic autoimmunity: murine acquired immunodeficiency syndrome (MAIDS), chronic graft-versus-host disease (cGVHD), and collagen-induced arthritis (CIA) to determine whether increases in B-1 cell frequency are universally seen in models of autoimmunity which are mechanistically distinct. In contrast to the aforementioned human systemic autoimmune diseases which exhibit an increase in CD5+ B cell frequency, the percentage of CD5+ B cells declined in all three murine models of systemic autoimmune disease. Even though there was a decrease in the frequency of CD5+ B cells there was no change in the actual number of CD5+ B cells. Thus, the apparent decline in CD5+ B cell frequency was due to increases in either T cells, conventional Fc epsilon R+ B cells, or both. The only actual decline in a B cell subset was the loss of IgM+, Fc epsilon Rdu11 cells in both the spleen and peritoneal cavity of mice undergoing a chronic graft-versus-host reaction. Therefore, our data suggests that expansion of the B-1 subset does not occur as a general feature of murine systemic autoimmune disease. These observations, consistent with previous studies of Ig gene usage in autoreactive **antibodies**, support the view that expansion and differentiation of the CD5- B cell subset is not a central event leading to autoantibody production.

=> dup remove l23

PROCESSING COMPLETED FOR L23

L26 37 DUP REMOVE L23 46 DUPLICATES REMOVED.

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L26 ANSWER 1 OF 37 MEDLINE DUPLICATE 1
2062200719 Document Number: 21904109. PubMed ID: 11906504. Increased expression of the neuronal glutamate transporter (EAAT3/EAAC1) in hippocampal and neocortical epilepsy. Crino Peter B; Jin Hong; Shumate Melissa D; Robinson Michael B; Coulter Douglas A; **Brooks-Kayal Amy R.** (PENN Epilepsy Center, Department of Neurology, University of Pennsylvania, Philadelphia, Pennsylvania, USA.) **EPILEPSIA**, (2002 Mar) 43 (3) 211-8. Journal code: 2983306R. ISSN: 0013-9580. Pub. country: United States. Language: English.

AB PURPOSE: To define the changes in gene and protein expression of the neuronal glutamate transporter (EAAT3/EAAC1) in a rat model of temporal lobe epilepsy as well as in human hippocampal and neocortical epilepsy. METHODS: The expression of EAAT3/EAAC1 mRNA was measured by reverse Northern blotting in single dissociated hippocampal dentate granule cells from rats with pilocarpine-induced temporal lobe epilepsy (TLE) and age-matched controls, in dentate granule cells from hippocampal surgical specimens from patients with TLE, and in dysplastic neurons microdissected from human focal cortical dysplasia specimens. Immunolabeling of rat and human hippocampi and cortical dysplasia tissue with EAAT3/EAAC1 antibodies served to corroborate the mRNA expression analysis. RESULTS: The expression of EAAT3/EAAC1 mRNA was increased by nearly threefold in dentate granule cells from rats with spontaneous seizures compared with dentate granule cells from control rats. EAAT3/EAAC1 mRNA levels also were high in human dentate granule cells from patients with TLE and were significantly elevated in dysplastic neurons in cortical dysplasia compared with non-dysplastic neurons from postmortem control tissue. No difference in expression of another glutamate transporter, EAAT2/GLT-1, was observed. Immunolabeling demonstrated that EAAT3/EAAC1 protein expression was enhanced in dentate granule cells from both rats and humans with TLE as well as in dysplastic neurons from human cortical dysplasia tissue. CONCLUSIONS: Elevations of EAAT3/EAAC1 mRNA and protein levels are present in neurons from hippocampus and neocortex in both rats and humans with epilepsy. Upregulation of EAAT3/EAAC1 in hippocampal and neocortical epilepsy may be an important modulator of extracellular glutamate concentrations and may occur as a response to recurrent seizures in these cell types.

L26 ANSWER 2 OF 37 MEDLINE DUPLICATE 2
2001183114 Document Number: 21128425. PubMed ID: 11233905. Improved flow cytometric detection of HLA alloantibodies using pronase: potential implications in renal transplantation. Vaidya S; Cooper T V; Avandsalehi J; Barnes T; **Brooks K**; Hymel P; Noor M; Sellers R; Thomas A; Stewart D; Daller J; Fish J C; Gugliuzza K K; Bray R A. (Department of Pathology, University of Texas Medical Branch, Galveston 77555-0178, USA.) **TRANSPLANTATION**, (2001 Feb 15) 71 (3) 422-8. Journal code: 01321444. ISSN: 0041-1337. Pub. country: United States. Language: English.

AB BACKGROUND: Flow cytometric crossmatch (FCXM) has grown in popularity and has become the "standard of practice" in many programs. Although FCXM is the most sensitive method for detecting alloantibody, the B cell FCXM has been problematic. Difficulties with the B cell FCXMs have been centered around high nonspecific fluorescence background owing to Fc-receptors present on the B cells and autoantibodies. To improve the specificity and sensitivity of the B cell FCXM, we utilized the proteolytic enzyme pronase to remove Fc receptors from lymphocytes before their use in FCXM. METHODS: Lymphocytes isolated from peripheral blood, spleen, or lymph nodes were treated with pronase and then used in a three-color FCXM. A total of 16⁺ T- and B cell FCXMs using pronase-treated and untreated cells were performed. Testing used serial dilutions of HLA alleles a 22 class I and 6

class II), with the titer of each **antibody** at one dilution past the titer at which the complement-mediated cytotoxicity anti-human globulin crossmatch became negative. RESULTS: After pronase treatment, the actual channel values of the negative control in both T cell and B cell FCXMs declined from 78+/-10 to 57+/-4 ($P<0.05$) and 107+/-11 to 49+/-3 ($P<0.00001$), respectively. Pronase treatment resulted in improved sensitivity of the T and B cell FCXM in detecting class I **antibody** by 20% and 80%, respectively. In no instance was a false-positive reaction observed. In this study, pronase treatment improved the specificity of B cell FCXM for detecting class II **antibodies** from 75% to 100% ($P=0.03$). In no instance was a false-negative reaction recorded. Lastly, on the basis of these observations we re-evaluated three primary transplant recipients who lost their allografts because of accelerated rejection. One of the patients was transplanted across negative T and B cell FCXM, whereas the other two patients were transplanted across a positive T cell, but negative B cell, FCXM. After pronase treatment, T and B cell FCXMs of each patient became strongly positive, and donor-specific anti-HLA class I **antibody** was identified in each case. CONCLUSION: Utilization of pronase-treated lymphocytes improves both the sensitivity and specificity of the FCXM.

L26 ANSWER 3 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:495043 Document No.: PREV200000495164. Influenza vaccine may induce auto-reactive IgG **antibodies** detectable in flow cytometry crossmatches. Cooper, T. Y. (1); Avandsalehi, J. (1); Hymel, P. (1); Barnes, T. (1); Thomas, A. (1); Sellers, R. (1); **Brooks, K. (1)**; Noor, M. (1); Qiu, S. M. (1); Gugliuzza, K. (1); Daller, J. (1); Vaidya, S. (1). (1) Departments of Pathology and Surgery, University of Texas Medical Branch, Galveston, TX USA. Human Immunology, (2000) Vol. 61, No. Supplement 2, pp. S80. print. Meeting Info.: 26th Annual Meeting of the American Society for Histocompatibility and Immunogenetics Lake Buena Vista, Florida, USA October 10-14, 2000 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English. Summary Language: English.

L26 ANSWER 4 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1999:472830 Document No.: PREV199900472830. High background fluorescence may contribute to false negative B lymphocyte flow cytometry crossmatches. Cooper, T. (1); Hymel, P. (1); Thomas, A. (1); **Brooks, K. (1)**; Avandsalehi, J. (1); Stewart, D.; Bray, R.; Vaidya, S. (1). (1) Department of Pathology, The University of Texas Medical Branch, Galveston, TX USA. Human Immunology, (1999) Vol. 60, No. SUPPL. 2, pp. S140. Meeting Info.: 25th Annual Meeting of the American Society for Histocompatibility and Immunogenetics New Orleans, Louisiana, USA October 20-24, 1999 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 5 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
1998:483339 The Genuine Article (R Number: ZU942. Modulation of IL-1 beta, IL-6 and TNF-alpha secretion and mRNA expression by the trichothecene vomitoxin in the RAW 264.7 murine macrophage cell line. Wong S S; Zhou H R; MarinMartinez M L; **Brooks K**; Pestka J J Reprints. MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, 234 GM TROUT BLDG, E LANSING, MI 48824 Reprint ; MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, E LANSING, MI 48824; MICHIGAN STATE UNIV, INST ENVIRONM TOXICOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, NATL CTR FOOD SAFETY & TOXICOL, E LANSING, MI 48824. FOOD AND CHEMICAL TOXICOLOGY MAY 1998 Vol. 36, No. 5, pp. 419-419. Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, WILLINGTON, OXFORD OX5 1GB, ENGLAND. ISSN: 0278-6918. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND CALL FORMATS

AB Oral exposure of mice to vomitoxin NT has been previously shown to

enhance gene expression of several cytokines associated with macrophage activation. Here, the effects of exposure to VT in vitro on cytokine secretion and mRNA expression were determined in the murine macrophage cell line RAW 264.7. Enzyme-linked immunosorbent assay (ELISA) of supernatants revealed that significant increases in secreted tumour necrosis factor alpha (TNF-alpha) were observed 2 days after exposure to VT at 100 ng/ml and 250 ng/ml, both with and without lipopolysaccharide (LPS) activation. While VT did not affect IL-6 secretion in the absence of LPS, significantly increased IL-6 production was observed in culture supernatants after 1, 2 and 5 days of exposure to VT at 250 ng/ml in the presence of LPS. Soluble IL-1 beta was not detected in control or VT-treated cell cultures with or without LPS activation. Immunohistochemical staining of intracellular cytokines in conjunction with flow cytometric analysis was used to detect the effects of VT on the percentage of positive cells and output per cell. The percentage of cells that produced intracellular TNF-alpha were significantly increased at 100 and 250 ng/ml VT with and without LPS whereas increased IL-6 output per cell was observed at 100 and 250 ng/ml VT with LPS. To assess the effects of VT on cytokine mRNA expression, RAW 264.7 cells were analysed semi-quantitatively using reverse transcription-polymerase chain reaction (RT-PCR) in conjunction with Southern hybridization analysis. Elevated TNF-alpha mRNA was observed at 100 and 250 ng VT/ml at 6 and 24 hr in the absence of LPS. With the addition of LPS, superinduction of TNF-alpha was not observed in the presence of VT. Increased IL-1 beta and IL-6 mRNAs were observed at 100 and 250 ng VT/ml at 24 hr in the presence of LPS. These results demonstrated that VT could superinduce both cytokine secretion and mRNA levels in macrophage cultures. (C) 1998 Elsevier Science Ltd. All rights reserved.

L26 ANSWER 6 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
 1998:182785 The Genuine Article (R) Number: Y2186. Role of macrophages in elevated IgA and IL-6 production by Peyer's patch cultures following acute oral vomitoxin exposure. Yan D (Reprint); Zhou H R; Brooks K H; Pestka J J. MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, E LANSING, MI 48824 (Reprint); MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, INST ENVIRONM TOXICOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, NATL FOOD SAFETY & TOXICOL, E LANSING, MI 48824. TOXICOLOGY AND APPLIED PHARMACOLOGY (FEB 1998) Vol. 148, No. 2, pp. 261-273. Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS. 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495. ISSN: 0041-008X. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Oral vomitoxin (VT) exposure in mice results in elevated cytokine gene expression, increased production of IgA, and IgA nephropathy. To determine the potential role of macrophages (M phi) in these effects, an ex vivo model was devised whereby Peyer's patch (PP) and spleen cells were prepared from mice 2 h after oral exposure to 0 or 25 mg/kg body wt VT, cultured, and then evaluated for IgA and cytokine IL-6 production. Both PP and, to a lesser extent, spleen cells from treatment mice produced more IgA over a 7-day period than did corresponding control cells when cultured without a costimulus or in the presence of either phorbol myristate acetate plus ionomycin (PMA + ION) or lipopolysaccharide (LPS). IgA elevation was most marked in LPS-treated cultures. The VT effect was completely ablated in PP cultures that were depleted of M phi but not in M phi-depleted spleen cultures. VT exposure similarly increased production of IL-6, an important helper factor for IgA secretion, in LPS-stimulated PP and spleen cell cultures. IL-6 production was also ablated by M phi depletion. A potential costimulatory role for M phi was further suggested because both IgA and IL-6 production increased when M phi-depleted PP cells from VT-treated animals were recultured with peritoneal M phi from VT-treated animals. Similar effects were observed when an analogous ex vivo approach was used with purified PP B cells and peritoneal M phi. PP B cells from control animals also secreted elevated levels of IgA when

cocultured with splenic CD4⁺ cells from VT-treated animals, thus confirming previous studies showing that T cell help also contributes to increased IgA production. Potential roles for soluble mediators and cell contact in this process were suggested when IgA production was measured in cultures of PP cells separated from VT-treated M phi by a semipermeable membrane. Taken together, these and previous results suggest that M phi may play a key mechanistic role in elevated IgA production and IgA nephropathy in VT-exposed mice. C 1998 Academic Press.

L26 ANSWER 7 OF 37 MEDLINE DUPLICATE 3
1998432619 Document Number: 98432619. PubMed ID: 9761452. The glutamate transporter, GLT-1, is expressed in cultured hippocampal neurons.

Brooks-Kayal A R; Munir M; Jin H; Robinson M B. (Department of Neurology, Children's Hospital of Philadelphia, Children's Seashore House, University of Pennsylvania, 19104, USA.. kayal@email.chop.edu) . NEUROCHEMISTRY INTERNATIONAL, (1998 Aug) 33 (2) 95-100. Journal code: 8006959. ISSN: 0197-0186. Pub. country: ENGLAND: United Kingdom. Language: English.

AB There are multiple subtypes of Na⁺-dependent glutamate transporters. Several studies suggest that EAAC1 and EAAT4 are expressed in neurons, while GLT-1 and GLAST expression is thought to be restricted to glia. In the present study, expression of GLT-1 and EAAC1 was examined in cultured rat hippocampal neurons using single cell mRNA amplification and immunocytochemistry with subtype specific antibodies. GLT-1 and EAAC1 mRNAs were observed in all neurons examined. Neuronal phenotype was confirmed in these cells by expression of neurofilament (NF-L) mRNA and absence of glial fibrillary acidic protein (GFAP) mRNA. EAAC1 immunoreactivity was observed in essentially all cells which expressed neuron specific enolase (NSE) and GLT-1 immunoreactivity was detected in the majority (approximately 90%) of NSE-positive cells. Consistent with the glial expression of GLT-1, GLT-1 immunoreactivity was also observed in NSE-negative cells. These studies provide evidence that GLT-1 expression is not intrinsically restricted to glial cells, but can occur in neurons under certain circumstances.

L26 ANSWER 8 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:470990 Document No.: PREV199800470990. Impact of positive flow crossmatches on primary renal transplants. Cooper, Todd; Vaidya, Smita; Asfour, M. Ayman; Avandsalehi, Jeanne; Barnes, Titus; **Brooks, Karl**; Lopez, Sheila; Partlow, David; Sellers, Racheal; Thomas, Alice. Univ. Tex. Med. Branch, Galveston, TX USA. Human Immunology, (1998) Vol. 59, No. SUPPL. 1, pp. 7. Meeting Info.: 24th Annual Meeting of the American Society for Histocompatibility and Immunogenetics Vancouver, British Columbia, Canada October 10-15, 1998 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 9 OF 37 MEDLINE DUPLICATE 4
97418734 Document Number: 97418734. PubMed ID: 9274810. Potential role for IL-5 and IL-6 in enhanced IgA secretion by Peyer's patch cells isolated from mice acutely exposed to vomitoxin. Yan D; Zhou H R; **Brooks K H**; Pestka J J. Department of Food Science and Human Nutrition, Michigan State University, East Lansing 48824, USA. TOXICOLOGY, (1997 Sep 26) 122 (1-2) 145-58. Journal code: 0361055. ISSN: 0300-483X. Pub. country: Ireland. Language: English.

AB Dietary exposure to vomitoxin (VT) results in hyper-elevated serum IgA and IgA nephropathy in mice. To assess the possible role of cytokines in this IgA dysregulation, the effects of a single oral exposure in B6C3F1 male mice to 0, 5 or 25 mg/kg BW VT on production of IgA and cytokines in Peyer's patch (PP) and spleen cell cultures were evaluated. IgA levels were increased significantly in PP cell cultures prepared from mice at 0 or 24 h after oral exposure to VT and subsequently stimulated with phorbol myristate acetate (PMA) and ionomycin (ION) or with lipopolysaccharide (LPS). Significant effects on IgA production were not observed in spleen

cell cultures. Since cytokines such as IL-2, IL-4, IL-5 and IL-6 have been shown to promote IgA production, the effect of the same VT exposure regimen on secretion of these mediators was determined in PP and spleen cultures. Supernatant IL-2 and IL-4 levels were unaffected by the prior treatment of animals with VT. In contrast, IL-5 levels were increased significantly in 7-day PP cell cultures obtained 2 h after VT exposure both with and without PMA + ION exposure but not in other cultures. IL-6 levels were increased significantly in LPS-treated cultures prepared from PP at 2 and 24 h following exposure to VT. IL-6 levels were also elevated significantly in both PMA + ION or LPS treated cultures from spleen isolated at 2 h but not 24 h post VT exposure. To determine whether IL-5 or IL-6 play a role in IgA hypersecretion in vitro, PP and spleen cells from mice obtained 2 h after exposure to 25 mg/kg VT were cultured in the presence of neutralizing cytokine antibodies (Abs) and IgA production was monitored. Consistent with IL-5's previously documented role in IgA production, anti-IL-5 decreased IgA levels to background in cultures of both control and VT-exposed PP or spleen cells in the presence of either PMA + ION or LPS. Similar results were seen with addition of anti-IL-6. IgA levels were decreased to a lesser extent in PP cells cultured with LPS and in spleen cells cultured with PMA + ION from VT-exposed mice to which anti-IL-2 Ab was added. Thus, the potential for enhanced IgA production exists in lymphocytes as early as 2 h and as late as 24 h after a single oral exposure to VT and this may be related to the increased capacity to secrete helper cytokines of T cell and macrophage origin. Taken together, the results suggest that the superinduction of cytokine expression may, in part, be responsible for upregulation of IgA secretion in mice exposed orally to VT.

L26 ANSWER 10 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 1998:62941 Document No.: PREV19980062941. Acute rejection of a living related kidney associated with positive T-cell flow cytometry crossmatch. Cooper, T. Y.; Sellers, R. B.; Asfour, M. A.; Lopez, S. B.; Moller-Nichols, M.; Barnes, T. H.; Brooks, K.; Partlow, D.; Avandalehi, J.; Thomas, A.; Vaidya, S. Dep. Pathol., Univ. Texas Med. Branch, Galveston, TX USA. Human Immunology, (1997) Vol. 55, No. SUPPL. 1, pp. 75. Meeting Info.: 23rd Annual Meeting of the American Society for Histocompatibility and Immunogenetics Atlanta, Georgia, USA October 14-19, 1997 The American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 11 OF 37 MEDLINE DUPLICATE 5
 96022850 Document Number: 96022850. PubMed ID: 7549055. Clinical importance of pre-mortem blood lymphocytes in cadaver donor tissue typing. Vaidya S; Orchard P; Schroeder N; Haneke R; Brooks K; Thomas A; Corba A; Asfour A; Fish J C. (Department of Pathology, University of Texas Medical Branch, Galveston 77555 0546, U.S.A.) CLINICAL TRANSPLANTATION, (1995 Jun) 9 (3 Pt 1) 165-70. Journal code: 8710240. ISSN: 0902-0063. Pub. country: Denmark. Language: English.

AB We have refined our immunomagnetic bead (IM bead) procedures to isolate pure and viable lymphocyte subpopulation from pre-mortem (PM) blood for cadaver donor HLA typing, preliminary and final crossmatches (XMs). The results of 1220 XMs were compared using T/B lymphocytes isolated either from PM blood or spleen/lymphnode (SPLN) tissue. IM bead technique was used to isolate T/B cells from PM blood and nylon wool column (NWC) technique was used to isolate T/B cells from SPLN. When we compared the outcome of 800 T-cell crossmatches using T cells from PM blood or SPLN of 5 separate cadaver donors, NWC TXMs tended to be more false negative for high PRA > 10%, total 800 XMs as well as low PRA < 10%, total 800 XMs did not reach statistical significance. In contrast, NW BXM 400 B XM were found to be far more false negative than IM bead BXM regardless of the PRA of the patients. In order to ensure that NWC BXMs were indeed false negative, 23 sera with known anti-DR antibodies were EXMed where antigen-specific B cells were isolated by both the techniques. Our

results showed that IM bead EXM identified the DR specificities greater than 90- of the time, the titers of ab specificities were stronger (1:8). In comparison, NWB cell XMs were weak (titers 1:2), and the false negative rate for some ab was as high as 73-. Using IM bead and NWC techniques we compared our turnaround time (TAT) for cadaver donor typing, preliminary and final XMs. (ABSTRACT TRUNCATED AT 250 WORDS)

L26 ANSWER 12 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 6
94251909 EMBASE Document No.: 1994251909. In vitro effects of vomitoxin (deoxynivalenol) on T-cell interleukin production and IgA secretion. Warner R.L.; Brooks K.; Pestka J.J. Dept. of Food Sci./Human Nutrition, 234 G.M. Trout Bldg., Michigan State University, East Lansing, MI 48824-1224, United States. Food and Chemical Toxicology 32/7 (617-625) 1994.

ISSN: 0278-6915. CODEN: FCTOD7. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The exposure of lymphocyte cultures to vomitoxin was used to determine possible mechanism by which this naturally occurring toxin induces serum immunoglobulin A (IgA) elevation and IgA nephropathy in the mouse. Vomitoxin exposure within the range of 10 to 1000 ng/ml inhibited DNA synthesis, protein synthesis as well as IgA, IgG and IgM production in lymphocyte cultures prepared from the Peyer's patch (PP) and spleen. When purified B cells were cultured in the presence of vomitoxin, inhibition of IgA, IgG and IgM production was similarly observed. However, on 24-hr pulsed co-exposure to vomitoxin and the mitogen concanavalin A (ConA), CD4+/CD8+ cells were capable of inducing a three- to five-fold increase in production of IgA, but not IgG and IgM by cocultured B cells when compared with B cells cocultured with control T cells exposed to the mitogen only. When pulsed for 48 hr with ConA and toxin, CD4+ cells were similarly capable of causing a significant increase in IgA production by B cells. 48-hr pulsed exposure of CD4+ cells to ConA and vomitoxin resulted in significantly increased production of the T helper cytokines IL-4, IL-5 and IL-6 after 5 additional days of culture, compared with ConA-stimulated CD4+ cells alone. These results suggest that vomitoxin was capable of enhancing CD4+-mediated help for IgA production by B cells and that this could possibly be mediated by way of increased cytokine production.

L26 ANSWER 13 OF 37 MEDLINE
94266212 Document Number: 94266212. PubMed ID: 8206429. Polyspecific and autoreactive IgA secreted by hybridomas derived from Peyer's patches of vomitoxin-fed mice: characterization and possible pathogenic role in IgA nephropathy. Rasooly L, Abouzied M M; Brooks K H; Pestka J J. (Department of Microbiology and Public Health, Michigan State University, East Lansing 48824.) FOOD AND CHEMICAL TOXICOLOGY, (1994 Apr) 32 (4) 337-48. Journal code: 8207483. ISSN: 0278-6915. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A total of 122 immunoglobulin (Ig)A-producing hybridoma clones were isolated from the Peyer's patches of vomitoxin-fed BALB/c mice and the resultant antibodies were characterized for their antigenic specificity and pathogenic potential. When reactivity was tested against a panel consisting of DNA, sphingomyelin, thyroglobulin, collagen, casein, cardiolipin and bovine serum albumin conjugates of phosphorylcholine, inulin and trinitrophenyl that were representative of self and non-self antigens, approximately 95% of the monoclonal IgAs bound to at least one of the panel antigens and 80% bound to more than one antigen. The polyspecificity of some of the monoclonal IgAs was further suggested by demonstrating the capacity of one antigen to inhibit binding of monoclonal IgA to another antigen. Protein staining and Western blotting of gradient native polyacrylamide gels, indicated that trimeric IgA predominated in the isolated monoclonal IgAs. Repeated injections of mice with representative monoclonal IgAs induced microhaematuria in three of four of the clones tested but not IgA deposition in the kidney glomerulus. In addition, three of the four monoclonal IgAs caused IgG and C3 deposition

in the kidney mesangium. These and previous results suggest that dietary vomitoxin promotes the polyclonal activation and expansion of IgA-secreting B cells at the Peyer's patch level and that resultant polyspecific, autoreactive IgA may contribute to kidney pathogenesis.

L26 ANSWER 14 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
94:364738 The Genuine Article (R) Number: HQ428. POLYSPECIFIC AND
AUTOREACTIVE IGA SECRETED BY HYBRIDOMAS DERIVED FROM PEYERS-PATCHES OF
VOMITOXIN-FED MICE - CHARACTERIZATION AND POSSIBLE PATHOGENIC ROLE IN IGA
NEPHROPATHY. RASCOOL L; ABOUZIED M M; **BROOKS K H**; PESTKA J J
(Reprint). MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, 234 GM TROUT
BLDG, E LANSING, MI, 48824 (Reprint); MICHIGAN STATE UNIV, DEPT FOOD SCI &
HUMAN NUTR, E LANSING, MI, 48824; MICHIGAN STATE UNIV, DEPT MICROBIOL &
PUBL HLTH, E LANSING, MI, 48824. FOOD AND CHEMICAL TOXICOLOGY (APR 1994)
Vol. 32, No. 4, pp. 337. ISSN: 0278-6915. Pub. country: USA. Language:
ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A total of 122 immunoglobulin (Ig)A-producing hybridoma clones were isolated from the Peyer's patches of vomitoxin-fed BALB/c mice and the resultant **antibodies** were characterized for their antigenic specificity and pathogenic potential. When reactivity was tested against a panel consisting of DNA, sphingomyelin, thyroglobulin, collagen, casein, cardiolipin and bovine serum albumin conjugates of phosphorylcholine, inulin and trinitrophenol that were representative of self and non-self antigens, approximately 95% of the monoclonal IgAs bound to at least one of the panel antigens and 80% bound to more than one antigen. The polyspecificity of some of the monoclonal IgAs was further suggested by demonstrating the capacity of one antigen to inhibit binding of monoclonal IgA to another antigen. Protein staining and Western blotting of gradient native polyacrylamide gels, indicated that trimeric IgA predominated in the isolated monoclonal IgAs. Repeated injections of mice with representative monoclonal IgAs induced microhaematuria in three of four of the clones tested but not IgA deposition in the kidney glomerulus. In addition, three of the four monoclonal IgAs caused IgG and C3 deposition in the kidney mesangium. These and previous results suggest that dietary vomitoxin promotes the polyclonal activation and expansion of IgA-secreting B cells at the Peyer's patch level and that resultant polyspecific, autoreactive IgA may contribute to kidney pathogenesis.

L26 ANSWER 15 OF 37 MEDLINE DUPLICATE 8
95048595 Document Number: 95048595. PubMed ID: 7525472. B-1 cells in systemic autoimmune responses: IgM+, Fc epsilon Rdu11 B cells are lost during chronic graft-versus-host disease but not in murine AIDS or collagen-induced arthritis. Iciek L A; Waldschmidt T J; Griffiths M M; **Brooks K H**. (Department of Microbiology, Michigan State University, East Lansing 48824.) IMMUNOLOGICAL INVESTIGATIONS, (1994 Aug) 23 (4-5) 293-311. Journal code: 8504629. ISSN: 0882-6139. Pub. country: United States. Language: English.

AB The potential role of B-1 cells [i.e. the CD5+ B cell and "sister" B cell subsets] in autoimmunity is controversial. CD5+ B cells have been shown to secrete **antibodies** of similar specificity as those found in many systemic autoimmune diseases; in addition, increases in CD5+ B cell frequency have been reported in patients suffering from rheumatoid arthritis, Sjogren's syndrome, myasthenia gravis, insulin-dependent diabetes mellitus and Hashimoto's thyroiditis. Whether these increases are due to expansion of B-1 lineage cells in the human or due to activation-induced expression of CD5 by conventional B cells is unclear. In the present study, we used three murine models of systemic autoimmunity: murine acquired immunodeficiency syndrome (MAIDS), chronic graft-versus-host disease (GVHD), and collagen-induced arthritis (CIA) to determine whether increases in B-1 cell frequency are universally seen in models of autoimmunity which are mechanistically distinct. In contrast to the aforementioned human systemic autoimmune diseases which exhibit an

increase in CD5+ B cell frequency, the percentage of CD5+ B cells declined in all three murine models of systemic autoimmune disease. Even though there was a decrease in the frequency of CD5+ B cells there was no change in the actual number of CD5+ B cells. Thus, the apparent decline in CD5+ B cell frequency was due to increases in either T cells, conventional Fc epsilon R+ B cells, or both. The only actual decline in a B cell subset was the loss of IgM+, Fc epsilon Rnull cells in both the spleen and peritoneal cavity of mice undergoing a chronic graft-versus-host reaction. Therefore, our data suggests that expansion of the B-1 subset does not occur as a general feature of murine systemic autoimmune disease. These observations, consistent with previous studies of Ig gene usage in autoreactive **antibodies**, support the view that expansion and differentiation of the CD5+ B cell subset is not a central event leading to autoantibody production.

- L26 ANSWER 16 OF 37 MEDLINE DUPLICATE 9
94045239 Document Number: 94045239. PubMed ID: 8228625. Cytotoxic cell proteinase gene expression and cytolytic activity by anti-CD3-activated cytotoxic T lymphocytes is sensitive to cyclosporin A but is not dependent on interleukin-2 synthesis. Kaiser M; Brooks-Kaiser J; Fitzpatrick LJ; Bleackley R C; Hoskin D W. (Department of Microbiology and Immunology, Dalhousie University, Halifax, Nova Scotia, Canada.) JOURNAL OF LEUKOCYTE BIOLOGY, (1993 Nov) 54 (5) 458-64. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.
- AB We have examined the role of interleukin (IL) 2 in the expression of cytotoxic cell proteinases (CCP) 1 and 2, as well as in the induction of major histocompatibility complex (MHC)-unrestricted cytotoxic activity in murine T cell cultures following stimulation with anti-CD3 monoclonal **antibody**. A dramatic reduction in CCP-1 and CCP-2 gene expression and near absence of cytolytic activity was shown to occur in these cultures when the expression of IL-2 was inhibited by 10(-6) M cyclosporin A (CsA). The inhibitory effect of CsA could not be eliminated by the addition to culture of recombinant IL-2 at concentrations typically present in anti-CD3-stimulated T cell culture supernatants. Furthermore, when endogenous IL-2 (45-60 U/ml) present in anti-CD3-stimulated T cell cultures was neutralized with anti-mouse IL-2 **antibody** there was no effect on CCP-1 and CCP-2 mRNA expression and only a slight decrease in cytolytic activity. The expression of CCP-1 and CCP-2 gene products and the induction of MHC-unrestricted cytotoxic activity in anti-CD3-stimulated T cell cultures therefore occur independently of IL-2 synthesis but are regulated by a CsA-sensitive mechanism.

- L26 ANSWER 17 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
93:126212 The Genuine Article (R) Number: KP121. COMPARISON OF THE INDUCTION OF ENDOTOXIN TOLERANCE IN ENDOTOXEMIA AND PERITONITIS BY MONOPHOSPHORYL LIPID-A AND LIPOPOLYSACCHARIDE. ASTIZ M E (Reprint); SAHA D C; BROOKS K; CARPATI C M; RACKOW E C. ST VINCENTS HOSP & MED CTR, NEW YORK MED COLL, DEPT MED, 153 W 11TH ST, NEW YORK, NY, 10011 (Reprint). CIRCULATORY SHOCK (MAR 1993) Vol. 39, No. 3, pp. 194-198. ISSN: 0092-6213. Pub. country: USA. Language: ENGLISH.

- *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
- AB We compared the induction of endotoxin tolerance with *Salmonella* minnesota monophosphoryl lipid A (MPL), a nontoxic derivative of lipid A, and *S. minnesota* endotoxin (LPS) in lethal endotoxemia and peritonitis. Lethal endotoxemia was induced by injecting 750 mug/mouse LPS intravenously. Cecal ligation and perforation was used to induce peritonitis. Tumor necrosis factor (TNF) was measured by immunoassay at 2 hr after lethal endotoxin infusion and 24 hr after peritonitis. A dose of 0.1 mug/mouse of MPL or LPS significantly reduced endotoxin mortality from 100% to 50% and 33%, respectively ($P < .05$). The LPS for a 0.1 mug dose of MPL was 75 mug of LPS and the LPS for a 0.1 mug dose of LPS was 1150 mug of endotoxin. $P < .05$. TNF levels decreased linearly when increasing doses of MPL and LPS were used to induce tolerance. At higher pretreatment

doses of LPS, survival benefits were attenuated despite the reduction in TNF levels. A 25 mug dose of LPS reduced mortality from peritonitis from 93- to 45- ($P < 0.05$). Although MPL reduced short-term mortality, overall mortality was not significantly reduced despite using large doses of MPL. TNF levels peaked at 24 hr and were significantly lower than those following lethal endotoxemia. The induction of endotoxin tolerance by LPS and MPL is dose dependent, and LPS is modestly more effective in inducing endotoxin tolerance than MPL. Both LPS and MPL are significantly less effective in protecting against lethality from peritonitis.

L26 ANSWER 18 OF 37 MEDLINE DUPLICATE 10
94096351 Document Number: 94096351. PubMed ID: 8271238. Inhibition of DNA synthesis and IL-2 bioactivity in MLR by splenic pregnancy-associated natural suppressor cells involves the production of a TGF-beta 1-like molecule and a second distinct inhibitory factor. **Brooks-Kaiser J C**; Hoskin D W. (Department of Microbiology and Immunology, Dalhousie University, Halifax, Nova Scotia, Canada.) JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1993 Sep) 25 (1) 31-49. Journal code: 8001906. ISSN: 0165-0378. Pub. country: Ireland. Language: English.

AB Natural suppressor cells exhibiting a double-negative, immature T cell phenotype have been identified in maternal spleen during syngeneic murine pregnancy. In the present study, splenic pregnancy-associated natural suppressor (SPANS) cells are shown to express alpha/beta T cell receptors. SPANS cell-mediated inhibition of DNA synthesis by spleen cells responding in mixed lymphocyte reactions (MLR) is associated with a reduction in interleukin (IL)-2 bioactivity beginning after 96 h of culture. Although culture supernatants from suppressed MLR exhibit diminished ability to support the growth of IL-2-dependent CTL-L2 cells, SPANS cells themselves are unable to inhibit IL-2-driven CTL-L2 proliferation, suggesting that SPANS cells down-regulate IL-2 synthesis in MLR. IL-2 utilization in MLR is also inhibited by SPANS cells, since the addition of exogenous IL-2 fails to relieve the inhibitory effect of SPANS cells on lymphoproliferative responses in MLR. Flow cytometric analysis reveals that MLR performed in the presence of SPANS cells contain normal percentages of CD4 and IL-2 receptor-bearing spleen cells. Thus, SPANS cells do not inhibit cellular proliferation in MLR by selectively interfering with clonal expansion of IL-2-producing helper T cells or by down-regulating IL-2 receptor expression. We have determined that SPANS cells inhibit DNA synthesis in MLR via the production of a transforming growth factor (TGF)-beta 1-like suppressor factor, since cellular proliferation in MLR is restored to normal levels in the presence of anti-TGF-beta 1 neutralizing antibody. However, IL-2 bioactivity in these cultures remains low in comparison to control MLR, suggesting the presence of a second distinct suppressor factor. Although the identity of this second inhibitory molecule has yet to be determined, neutralizing antibody studies have ruled out IL-10.

L26 ANSWER 19 OF 37 MEDLINE DUPLICATE 11
92308750 Document Number: 92308750. PubMed ID: 1535357. Soybean agglutinin-positive natural suppressor cells in mouse bone marrow inhibit interleukin 2 production and utilization in mixed lymphocyte reactions. **Hoskin D W**; Bowser D A; **Brooks-Kaiser J C**. (Department of Microbiology, Dalhousie University, Halifax, Nova Scotia, Canada.) JOURNAL OF LEUKOCYTE BIOLOGY, (1992 Jun) 51 6 649-56. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.
AB Although natural suppressor NS cells resident in bone marrow BM have been the subject of intensive study, the exact nature and mode of action of these potentially important immunoregulatory cells are still uncertain. Here we show that NS cells with potent inhibitory effects on mixed lymphocyte reactions MLRs can be isolated from BM of normal adult mice by agglutination with the plant lectin soybean agglutinin SEA. Complement-dependent lysis of SEA receptor-bearing BM cells with antibodies to asialoGM1, Mac-1, Thy-1.2, J1d.2, and 2c1

phenotypic markers reveals the presence of at least two distinct populations of BM NS cells. Most of the SBA-binding BM cells with NS capacity have the null phenotype and resemble hematopoietic stem cells, and some inhibitory SBA+ BM cells express the 2C1 marker found on pregnancy-associated splenic NS cells and the J11d.2 antigen characteristic of B cells and immature T cells. Results of positive selective experiments confirmed these findings. The mechanism of natural suppression was also studied. Evidence is presented that SBA+ BM cells exert NS activity in MLRs by interfering with the production and utilization of interleukin 2. Indomethacin does not relieve natural suppression associated with SBA+ BM cells, indicating that prostaglandin synthesis is not a requirement for inhibitory function. However, neutralizing **antibodies** to transforming growth factor beta (TGF-beta) partially reverse the suppression mediated by SBA+ BM cells, suggesting that some BM NS cells may act through the release of an immunosuppressive molecule related to TGF beta.

L26 ANSWER 20 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
92:542319 The Genuine Article (R) Number: JM219. CD5 EXPRESSION IS MODULATED AS THE B-CELL MOVES THROUGH THE CELL-CYCLE. **BROOKS K H (Reprint)** ; YOL Y S; PESTKA J J. MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint). ANNALS OF THE NEW YORK ACADEMY OF SCIENCES (04 MAY 1992) Vol. 651, pp. 259-260. ISSN: 0077-8923. Pub. country: USA. Language: ENGLISH.

L26 ANSWER 21 OF 37 MEDLINE DUPLICATE 12
92299374 Document Number: 92299374. PubMed ID: 1535063. Reactivity of monoclonal **antibody** 1E5.B5 with a novel phenotypic marker expressed on a murine natural suppressor cell subset. Hoskin D W; **Brooks-Kaiser J C**; Kaiser M; Murgita R A. (Department of Microbiology, Dalhousie University, Halifax, Nova Scotia.) HYBRIDOMA, (1992 Apr) 11 (2) 203-15. Journal code: 8202424. ISSN: 0272-457X. Pub. country: United States. Language: English.

AB Natural suppressor (NS) cells are antigen-nonspecific, MHC-independent immunoregulatory cells that are typically found in murine bone marrow (BM), newborn (NB) mouse spleen, and in splenic tissue of adult mice during pregnancy and following cyclophosphamide (CY) treatment. There has been a pressing need for the development of NS cell-specific monoclonal **antibodies** (mAb) since NS cells are generally described as null cells which lack the usual phenotypic markers of mature T cells, B cells, and macrophages. Here we present evidence that mAb 1E5.B5, which was raised in rats against murine splenic pregnancy-associated NS (SPANS) cells, recognizes a unique antigenic marker expressed by some, but not all, murine NS cells. In the presence of complement, mAb 1E5.B5 effectively eliminates SPANS activity, and diminishes NS activity of CY-treated spleen cells in mixed lymphocyte reactions (MLR). However, cytotoxic pretreatment with mAb 1E5.B5 had minimal effects on NS activity of BM and NB spleen cells. We also show that pregnancy spleen cells and CY-spleen cells with moderate NS activity in MLR can be positively selected for by "panning" with mAb 1E5.B5. In contrast, only weakly inhibitory cells are isolated from BM and NB spleen by this procedure. Cellular ELISA and flow cytometry confirm that mAb 1E5.B5 has specificity for pregnancy spleen cells and CY-spleen cells, as well as for NB spleen and BM cell preparations. Western blot analysis reveals that mAb 1E5.B5 reacts with a novel 50 kDa NS cell-associated antigen which we have termed NS-1. The NS-1 antigen is not present on other null cells such as natural killer (NK) cells and natural cytotoxic (NC) cells since cytotoxic pretreatment of pregnancy spleen cells with mAb 1E5.B5 does not affect **antibody**-dependent cell-mediated cytotoxicity, NK or NC activity.

L26 ANSWER 22 OF 37 MEDLINE
91339487 Document Number: 91339487. PubMed ID: 1831408. IL-2 and IL-6 both induce mu S and J chain mRNA in a clonal B cell line, but differ in

- their cell-cycle dependency for optimal signaling. Takayasu H; **Brooks K H.** Genetics Program, Michigan State University, East Lansing 48824. CELLULAR IMMUNOLOGY, (1991 Sep) 136 (2) 472-85. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.
- AB We have found that a neoplastic Lyl+ B cell clone 'BCL1-3B3' can be stimulated to secrete IgM by a Th1-derived cytokine, IL-2, and/or by a Th2-derived cytokine, IL-5. At suboptimal concentrations these interleukins acted synergistically to enhance IgM secretion. Both IL-2 and IL-5 induced increases in microsecond and J chain mRNA levels. In the presence of both ILs, increases in microsecond and C chain mRNA were additive and paralleled increases in IgM secretion. Using cells synchronized at the G1/S border with excess thymidine or in early G1 using isoleucine-deficient media, IL-2 and IL-5 differed in their cell-cycle dependency for signal transmission. IL-5 appeared to act preferentially in late G1 of the cell cycle. In contrast, IL-2 stimulated S and G2 phase cells slightly more efficiently than cells in G1 of the cell cycle. Furthermore, a twofold increase in high-affinity IL-2R was observed as the cells entered S phase. The results suggest that although IL-2 and IL-5 can independently and additively induce differentiation of the Lyl+ BCL1-3B3 cells, they differ in their point of action during the cell cycle.
- L26 ANSWER 23 OF 37 MEDLINE
91007479 Document Number: 91007479. PubMed ID: 2145206. Elevated membrane IgA+ and CD4+ (T helper) populations in murine Peyer's patch and splenic lymphocytes during dietary administration of the trichothece vomitoxin (deoxynivalenol). Pestka J J; Dong W; Warner R L; Rasooly L; Bondy G S; **Brooks K H.** (Department of Food Science and Human Nutrition, Michigan State University, East Lansing 48824.) FOOD AND CHEMICAL TOXICOLOGY, (1990 Jun) 28 (6) 409-20. Journal code: 8207483. ISSN: 0278-6915. Pub. country: ENGLAND: United Kingdom. Language: English.
- AB Recent investigations indicate that dietary exposure to the trichothece vomitoxin increases total and antigen-specific serum immunoglobulin A (IgA) and glomerular IgA accumulation in mice. In this study, the effects of 25 ppm dietary vomitoxin on the histological and lymphocytic profile of component immune organs in the mucosal lymphocyte migratory pathway were evaluated in the B6C3F1 mouse. Vomitoxin administration resulted in marked stimulation of the size and frequency of germinal centres in Peyer's patches, mesenteric lymph nodes and the spleen. A slight increase in the percentage of B cells in the Peyer's patch was observed, although vomitoxin treatment had no effect on the percentage of B cells in the spleen. The percentage of IgA+ cells in Peyer's patches and spleen were approximately twice that of controls at 4, 8 and 12 wk of vomitoxin exposure whereas the percentage of IgG+ cells decreased in these two organs. Exposure to vomitoxin increased the percentage of T cells in Peyer's patches and the spleen. The percentage of CD4+ cells (T helper subset) increased slightly in Peyer's patches and more markedly (30-50%) in the spleen following vomitoxin treatment. Contrastingly, there was only a slight increase in the percentage of CD8+ cells (T cytotoxic/suppressor subset) in the spleens of vomitoxin-treated mice in comparison with controls, and no effect in Peyer's patches. The relative effects of vomitoxin on these two T cell populations was also reflected in increased CD4+: CD8+ ratios in Peyer's patches and spleen. These results are consistent with the hypothesis that dietary vomitoxin modulates normal regulation of the IgA response at the Peyer's patch level and that this is manifested in an altered lymphocyte distribution pattern in both the mucosal and systemic compartment. Notably increased levels of IgA+ and CD4+ cells are indicative of IgA-producing progenitors and T helper subsets, respectively, that in tandem could favour IgA hyperproduction and elevated IgA in serum.

LYMPHOKINES. BROOKS K H (Reprint); OAKLEY C S; TAKAYASU H. MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint). JOURNAL OF MOLECULAR AND CELLULAR IMMUNOLOGY 1990; Vol. 4, No. 6, pp. 339-348. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recent advances of T cell cloning have allowed the classification of T helper cells in terms of the lymphokines they secrete. The functional significance of segregating lymphokine production to unique T cell subsets is still being evaluated, but undoubtedly plays a key role in the regulatory mechanisms of the immune system. Initial studies have indicated that the Th1 cells which secrete IL-2 and IFN-gamma may be primarily responsible for augmenting cell-mediated responses, whereas Th2 cells, which release IL-4, IL-5, and IL-6, provide help for humoral responses. However, it is also known that B cells can respond to both IL-2 and IFN-gamma. This raises the question of the homogeneity of B lymphocyte activation requirements. Are all B cells responsive to all of the lymphokines with the end-result of stimulation depending largely on the relative concentrations of the various lymphokines, or are there B cell subsets which only respond to Th1-derived lymphokines and others which respond to Th2-derived lymphokines? Such differential activation requirements might be present to allow these subsets to play unique roles in immunological responses. Since B cell cloning techniques have not yet been developed to obtain a homogenous B cell population for studies of activation requirements, regulation of lymphokine receptors, and regulation of gene expression, we must utilize lymphokine-responsive neoplastic B cells. The vast majority of spontaneous B cell lymphomas appear to belong to a minor B cell subset which expresses the Lyl marker. This subset is clearly not representative of the majority of splenic B cells. In this report, we have characterized the lymphokine response pattern of Lyl- B cell clones derived from a spontaneous tumor occurring in an AKR mouse.

Neoplastic B cell clones were generated from the 225 lymphoma, which secrete significant levels of IgM upon stimulation with lymphokines produced by type 2 T helper (Th2) cells. The 225 clones expressed a high-density of mIgM, varying densities of mIgD, and were mIgG and Lyl negative. Th2-derived lymphokines found in D10.G4.1 SN will induce differentiation, as indicated by release of IgM in the culture SN. The 225 cells did not respond to IL-2, IFN-gamma, IL-1, or any combination of these lymphokines. Optimal differentiation occurred only when IL-4, IL-5, and IL-6 were present. The order of differentiative activity of these lymphokines was IL-5 > IL-4 > IL-6. The lack of IL-2 responsiveness in the face of IL-2R-alpha (p55) chain expression was due to the lack of high-affinity IL-2 receptors. In contrast, the IL-2 responsive clone BCL1-3B3 expresses approximately 950 high affinity IL-2R per cell. Thus, the 225-11 clone should provide a useful model system for the evaluation of the regulation of immunoglobulin gene expression mediated by Th2-derived lymphokines.

L26 ANSWER 25 OF 37 SCISEARCH COPYRIGHT 2002 ISI /R
91:258713 The Genuine Article (R) Number: FJ252. ADRENOCORTICOTROPIN (ACTH) FUNCTIONS AS A LATE-ACTING B-CELL GROWTH-FACTOR AND SYNERGIZES WITH INTERLEUKIN-5. BROOKS K H (Reprint). MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint). JOURNAL OF MOLECULAR AND CELLULAR IMMUNOLOGY 1990; Vol. 4, No. 6, pp. 327-337. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In recent years there has been considerable discussion of possible cross-regulatory mechanisms involving the immune system and the neuroendocrine system. Certainly, evidence of hormonal communication between these two systems would provide at least a partial explanation for the many anecdotal observations of physical and mental stress affecting disease course. In previous studies of a neoplastic lymphokine-responsive B cell clone, BCL1-3B3, we noted that these cells produced a lymphokine

which could affect normal B cell growth and viability. Physical characterization of this lymphokine indicated that its molecular weight was identical to that of the neuroendocrine hormone adrenocorticotropin (ACTH). Since Blalock and colleagues had reported the production of ACTH by virally-infected B cells, we have investigated whether ACTH can functionally mimic the BCL1-3B3-derived lymphokine. The neuroendocrine hormone adrenocorticotropin (ACTH) can increase in vitro murine B lymphocyte proliferation when added at physiologically relevant concentrations between 10^{-9} to 10^{-11} M. ACTH does not mimic the action of any lymphokine known to be required for B cell proliferation such as IL-2, IL-4, or IL-5. ACTH requires the presence of one or more of these known B cell stimulatory factors for its action and the most marked increase in B cell proliferation were noted in assays for IL-5 activity where 10^{-10} M ACTH increased thymidine incorporation up to five-fold. Using two-stage assays, we determined that ACTH acts during the latter stages of B cell activation (i.e., 3-4 days after initial stimulation with either the combination of IL-4, GAMIG-Sepharose, and IL-1 or the combination of DMS and IL-5). These data indicate a direct role for a stress-induced neuroendocrine hormone in modulating the course of a humoral immune response.

L26 ANSWER 26 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

1987:262595 Document No.: BR33:4491. INTERLEUKIN-2 INDUCES IGM SECRETION IN LYL+ NEOPLASTIC B CELLS BCL-1. **BROOKS K H**; KRAMMER P H; UHR J W; VITETTA E S. DEP. MICROBIOL., UNIV. TEX. HEALTH SCI. CENTER, SOUTHWESTERN MED. SCH., DALLAS, TEX. 75235. GOLDSTEIN, G., J.-F. BACH AND H. WIGZELL (ED.). UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY NEW SERIES, VOL. 41. IMMUNE REGULATION BY CHARACTERIZED POLYPEPTIDES; STEAMBOAT SPRINGS, COLORADO, USA, JANUARY 25-FEBRUARY 1, 1986. XXVI+786P. ALAN R. LISS, INC.: NEW YORK, NEW YORK, USA. ILLUS. (1987) 0 (0), 305-314. CODEN: USMBD6. ISSN: 0735-9543. ISBN: 0-8451-2640-7. Language: English.

L26 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2002 ACS

1987:174381 Document No. 106:174381 Interleukin-2 induces IgM secretion in Lyl+ neoplastic B cells (BCL1). **Brooks, Kathryn H.**; Krammer, Peter H.; Uhr, Jonathan W.; Vitetta, Ellen S. (Southwest. Med. Sch., Univ. Texas, Dallas, TX, 75235, USA). UCLA Symp. Mol. Cell. Biol., New Ser., Volume Date 1986, 41(Immune Regul. Charact. Polypept.), 305-14 (English) 1987. CODEN: USMBD6. ISSN: 0735-9543.

AB Cells from 2 neoplastic B cell clones have been used to exam. the effect of interleukin-2 (IL-2) on B cell differentiation. Cells from both clones express high levels of secretory IgM but relatively little secretory IgD; however, they differ in their expression of the Lyl marker. The cells from the Lyl+ BCL1-derived (BALB/c) clone secrete IgM in response to purified and recombinant IL-2. This response can be blocked with monoclonal anti-IL-2 antibodies. In contrast, cells from a Lyl- neoplastic B cell clone from AKR mice (AKR-225) do not differentiate in response to IL-2 or IL-2 plus recombinant interferon. The cells from both the BCL1 clone and the AKR-225 clone can differentiate in response to B cell stimulatory factors present in supernatants of SNS of the alloreactive T cell line, PK 7.1. This PK 7.1 SNS lacks significant IL-2 activity but does contain the differentiation factor for IgM. The different activation requirements of these Lyl+ and Lyl- neoplastic B cells is intriguing in light of both the assocn. of normal Lyl+ B cells with autoimmune disease and the prodn. of a B cell growth factor by the Lyl+ BCL1 clone but not the AKR-225 clone.

L26 ANSWER 28 OF 37 MEDLINE

DUPLICATE 13

97034946 Document Number: 97034946. PubMed ID: 2845861. Recombinant IL 2 but not recombinant interferon-gamma stimulates both proliferation and IgM secretion in a Lyl- clone of neoplastic murine B cells BCL1. **Brooks K H**; Vitetta E S. JOURNAL OF IMMUNOLOGY, 1986 Nov 15 137

10. 3295-10. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
- AB We have used a lymphokine-responsive clone (3B3) of B leukemia cells (BCL1) to examine the effects of several recombinant and purified lymphokines. Cells from BCL1-3B3 were induced to secrete IgM in the presence of recombinant interleukin 2 (rIL 2) (10 to 50 U/ml); a concomitant increase in proliferation was observed. Recombinant interferon-gamma (rIFN-gamma) was a potent inhibitor of proliferation. In addition, rIFN-gamma did not induce an increase in IgM secretion and, when added to rIL 2-stimulated BCL1-3B3 cells, completely blocked IgM secretion at a concentration of 10 U/ml. Purified and recombinant IL 1 (rIL 1) had no significant effect on differentiation either alone or in combination with rIL 2 and/or rIFN-gamma. However, rIL 1 was able to synergize with rIL 2 in enhancing the proliferation of BCL1-3B3. The ability of cells to respond to rIL 2 was limited to the in vitro (Ly-1+) clones of BCL1 cells since the in vivo derived (Ly-1-) BCL1 cells did not differentiate in response to IL 2. Consistent with their functional response to rIL 2, cells from the in vitro clone (3B3) are IL 2-receptor-positive (IL-2R+) and the in vivo derived BCL1 cells are IL-2R-. A second set of neoplastic B cell clones derived from the AKR 225 lymphoma did not respond to rIL 2 even though they expressed receptors for IL 2 and could be induced by T cell supernatant to secrete IgM, thus indicating that expression of IL 2R is not the sole requirement for IL 2 responsiveness. The monoclonal anti-IL 2R antibody (7D4) mimicked IL 2 in its ability to stimulate differentiation of BCL1-3B3 cells. These data suggest that rIL 2 and the monoclonal anti-IL-2R antibody are capable of inducing a differentiative response in the Ly-1+ BCL1-3B3 cells that is functionally equivalent to the response evoked by the previously described lymphokine B cell differentiation factor for IgM (BCDF mu). Thus, two distinct lymphokines appear to be providing a similar signal to a clonal neoplastic B cell population. Furthermore, rIL 2 is capable of providing both a proliferative and a differentiative signal.
- L26 ANSWER 29 OF 37 MEDLINE
85081355 Document Number: 85081355. PubMed ID: 3871214. Cell cycle-related expression of the receptor for a B cell differentiation factor. **Brooks K H**; Uhr J W; Vitetta E S. JOURNAL OF IMMUNOLOGY, (1985 Feb) 134 (2) 742-7. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
- AB Cloned, neoplastic B cells (BCL1) have been used to evaluate the expression of the receptor for the B cell differentiation factor, BCDF mu. These cells do not secrete IgM before stimulation with BCDF mu-containing T cell supernatants (SN). By inducing cell cycle synchrony in this homogeneous population, the expression of the BCDF mu receptor could be evaluated as a function of the cell cycle. Responsiveness to BCDF mu-containing SN is maximal when the cells are in S and G2 phases of the cell cycle, and a 2-hr exposure of cells to BCDF mu-containing SN during S/G2 results in optimal IgM secretion 5 days later. Cells in S/G2 are also maximally effective in absorbing BCDF mu activity from SN. These data support the hypothesis that B cells do not respond to differentiative signals until after they are committed to at least one round of cell division.
- L26 ANSWER 30 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
8412729 EMBASE Document No.: 198412729. T cell-derived lymphokines that induced IgM and IgG secretion in activated murine B cells. Vitetta E.S.; **Brooks K.**; Chen Y.-N.; et al.. Department of Microbiology, University of Texas Health Science Center, Dallas, TX 75035, United States. Immunological Reviews 1984; 79:1-137-157. 1984.
CODEN: IMREDD. Pub. Country: Denmark. Language: English.
- AB We have defined 2 lymphokine activities, termed BCDF.mu. and BCDF.gamma., which are present in the supernatants of T cell tumors, lines and hybridomas. These lymphokines appear to act directly on activated normal B

cells (or in the case of BCGF.mu., on BCL1 cells as well) to induce the synthesis and secretion of IgM or IgG1, respectively. These lymphokines are different from each other as well as from IL-1, IL-2, IFN.gamma., and conventional TRF. By molecular weight, BCGF.mu. is different from BCGF. The 2 BCGFs appear to bind to 2 different receptors on the cell surface and, thereby, to induce changes in the levels of isotype-specific mRNA and secreted immunoglobulin. The binding of BCGF.mu. to target cells appears to be cell-cycle related (optimal in G2S) and independent of T cells and macrophages. This has not been proven for BCGF.gamma.. It is possible that a subset of cells present in normal B cell populations, but not represented by the cloned BCL1 cells, is needed for BCGF.gamma. activity. Studies from other laboratories describing BCGF.gamma. (Severinson et al. 1982) BCGF.alpha. (Mayer et al. 1982, Kawanishi et al. 1983), and BCGF.epsilon. (Kishimoto & Ishizaka 1973, Hirashima et al. 1981) activities in T cell supernatants suggest that T cell-derived lymphokines may regulate the expression and/or secretion of several classes of immunoglobulin in activated B cells.

L26 ANSWER 31 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1984:44777 Document No.: BR26:44777. LYMPHOKINE INDUCED DIFFERENTIATION OF CLONAL NEOPLASTIC B CELLS. **BROOKS K**; YUAN D; UHR J; KRAMMER P; VITETTA E S. UNIV. TEX. HEALTH SCI. CENT. DALLAS, DALLAS, TEX. 75235.. 67TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, CHICAGO, ILL., USA, APRIL 10-15, 1983. FED PROC. (1983) 42 (5), ABSTRACT #101. CODEN: FEPA7. ISSN: 0014-9446. Language: English.

L26 ANSWER 32 OF 37 MEDLINE
83192467 Document Number: 83192467. DUPLICATE 14
Lymphokine-induced IgM secretion by clones of neoplastic B cells.
Brooks K; Yuan D; Uhr J W; Krammer P H; Vitetta E S. NATURE, (1983 Apr 28) 302 (5911) 825-6. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The induction of antibody secretion by B cells requires T-cell-derived factors 1-5. Such factors have been described 1,2,6-12 but the precise relationship among these various factors is not clear, and it has been difficult to demonstrate that these factors act directly on the B cell and do not exert their effect via T cells or macrophages. In this report we describe the direct induction of IgM synthesis and secretion in cloned lines of long-term tissue culture adapted neoplastic B cells (BCL1) by T-cell supernatants from phorbol-12-myristate 13-acetate (PMA)-induced EL-4 cells or concanavalin A (Con A)-induced 7.1.1a cells. We have termed this activity BCGFmu (B-cell differentiation factor for IgM). The supernatants containing BCGFmu induce activated and neoplastic B cells to secrete IgM5 and the factor responsible is distinct from BCGF13, interleukin-2 (IL-2)5, the classical T-cell replacing factor (TRF) described by Schimpl and Wecker5, and immune interferon (IFN gamma)5.

L26 ANSWER 33 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 15
83152564 EMBASE Document No.: 1983152564. The correlation between the activation state of B cells and their capacity for in vitro propagation of immunologic memory. **Brooks K.H.**; Feldbush T.L. Dep. Microbiol., Univ. Iowa, Iowa City, IA 52242, United States. Cellular Immunology 76/2 213-223; 1983.

AB CODEN: CLIM88. Pub. Country: United States. Language: English.
The B-cell population responsible for in vitro antigen-mediated proliferation and expansion of the memory B-cell population is a large activated blast. Such cells predominate early after antigen priming and can be regenerated by adjuvant Bordetella pertussis stimulation in vivo. Although these cells are proliferating in vivo, additional stimuli are needed for expansion of the memory population in vitro. These triggering requirements include specific antigen, INF-gamma, and the assistance of adherent accessory cells. Although T cells are present in the culture,

their role in the propagation of memory is not completely clear. Using the unrelated antigen, sheep erythrocytes, we have shown that 'bystander' T-cell help can mediate differentiation of these memory B-cell blasts to AFC, but it cannot induce expansion of the memory-cell population. However, the fact that the T1-2 antigen DNP-Ficoll is a relatively ineffective inducer of memory-cell propagation (inducing an expanded response which is less than 10% of that induced by the T-cell-dependent antigen, DNP-OVA) suggests that T cells may be involved, possibly via production of B-cell growth factor. Thus, the minimal requirements for triggering the propagation of B-cell memory include (i) a blastogenic signal which can be mediated by adjuvant, (ii) specific antigen, and (iii) adherent accessory-cell help.

L26 ANSWER 34 OF 37 MEDLINE DUPLICATE 16
81265503 Document Number: 81265503. PubMed ID: 7021678. Generation of antibody-mediated regulation during in vitro clonal expansion of memory B lymphocytes. **Brooks K H**; Feldbush T L. JOURNAL OF IMMUNOLOGY, (1981 Sep) 127 (3) 963-7. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

L26 ANSWER 35 OF 37 MEDLINE
81265502 Document Number: 81265502. PubMed ID: 7021677. In vitro antigen-mediated clonal expansion of memory B lymphocytes. **Brooks K H**; Feldbush T L. JOURNAL OF IMMUNOLOGY, (1981 Sep) 127 (3) 959-63. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB An in vitro model for the propagation and expansion of the memory B lymphocyte population is described. DNP-BGG immune cells were mixed with OVA immune cells and challenged immediately with DNP-OVA. After the 1st response had begun to wane, the cells were rechallenged with DNP-OVA (day 11 of culture). An average of 13-fold more PFC were observed after delayed challenge (day 11). This expansion in the PFC response was an antigen-dependent process and did not involve recruitment of new memory cells from the virgin lymphocyte pool. The level of expansion of the memory cell pool was also calculated using limiting dilution analysis and was found to fall in a range of 16- to 67-fold increase in precursor frequency. In addition to the expansion of the memory B cell population, we also observed the development of 2 immunoregulatory cycles previously observed only in vivo. First, in the presence of persistent antigen, a cyclical PFC response was seen. Second, after day 10 of culture, optimal PFC numbers were observed only when DNP-lysine was added to the plaque assay. Such hapten-augmentable PFC responses have been reported by other investigators as indicative of anti-idiotypic regulation. This possibility is examined more extensively in the following communication.

L26 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2002 ACS
1982:558292 Document No. 97:158292 Isolation and characterization of an .alpha.1-antitrypsin-related glycoprotein from human liver. Glew, Robert H.; Zidian, J. L.; Chiao, J. P.; Kuhlenschmidt, T.; Iammarino, Richard M.; **Brooks, K. P.** (Sch. Med., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA). Electrophor. '81 [Eighty-One], Proc. Int. Conf., 3rd, 511-21. Editor s: Allen, Robert Chadbourne; Arnaud, Philippe. de Gruyter: Berlin, Fed. Rep. Ger. English 1981. CODEN: 48KUAG.

AB A 68,000-dalton glycoprotein which cross-reacts with antibody to human plasma .alpha.1-antitrypsin I was purified from the 100,000-g supernatant of human liver. This glycoprotein I-CRM had 8.5% of the immunoreactivity of I and no antiprotease activity. Isoelec. focusing resolved I-CRM into 2 fractions which differed in immunoreactivity. Carbohydrate and amino acid analyses were carried out. I-CRM, which differed from I in mol. wt., also differed substantially in CNBr- and chymotrypsin-derived fragments. The basis of the relatedness of plasma I and I-CRM, which represents only approx. 1.1% of liver protein content, is not known; however, as immunospecificity was the major criteria for

purifn. the report of frequent findings of I-CRM in normal and diseased liver may be accounted for by the present observation.

L26 ANSWER 37 OF 37 MEDLINE DUPLICATE 17
80132519 Document Number: 80132519. PubMed ID: 6153580. The generation of memory B-cell subpopulations capable of proliferation and expansion of the pool: effect of time and antigen. **Brooks K H**; Feldbush T L; van der Hoven A. CELLULAR IMMUNOLOGY, /1980 Mar 15; 50 /2; 392-404. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

=>

--Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
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CA SUBSCRIBER PRICE	ENTRY	SESSION
	-15.49	-15.49

STN INTERNATIONAL LOGOFF AT 13:29:54 ON 05 JUL 2002

1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. **Reff, Mitchell R.**; Barnett, Richard Spence; McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US 5598144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors (Molly) and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, N1+Neomycin phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human **CD23 antibody** and immunoadhesin in Desmond marked CHO cells was achieved.

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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
	15.21	15.42
DISCOUNT AMOUNTS FOR QUALIFYING ACCOUNTS	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY	SESSION
	-0.62	-0.62

STN INTERNATIONAL LOGOFF AT 14:43:09 ON 15 JUL 1999

=> dup remove L2
 PROCESSING COMPLETED FOR L2
 L3 3 DUP REMOVE L2 (6 DUPLICATES REMOVED)
 => d 13 1-3 cbib abs

L3 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
 2002224456 Document Number: 21957917. PubMed ID: 11962725. Anti-CD23
 monoclonal antibody inhibits germline Cepsilon transcription in B cells.
 Yabuuchi Shingo; Nakamura Takehiko; Kloetzer William S
 ; Reff Mitchell E. (Seikagaku Corporation, Central Research
 Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) .
 Int Immunopharmacol, (2002 Mar) 2 (4) 453-61. Journal code: 100965259.
 ISSN: 1567-5769. Pub. country: Netherlands. Language: English.
 AB A chimeric macaque/human (PRIMATIZED) anti-CD23 antibody
 , p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40
 antibody-stimulated IgE production by human peripheral blood mononuclear
 cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain
 reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline
 Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data
 suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE
 through the inhibition of germline Cepsilon RNA synthesis. Early addition
 of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE
 inhibition. In contrast, later addition of p6G5G1 still showed inhibition
 of increased levels of surface CD23, which is normally upregulated by
 stimulation with IL-4 and anti-CD40.

L3 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
 2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE
 inhibition in B cells by anti-CD23 monoclonal antibodies is functionally
 dependent on the immunoglobulin Fc domain. Nakamura T;
 Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J;
 Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E.
 (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.)
 INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41.
 Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND; United
 Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcεvarepsilonRII), is involved in
 regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies
 to human CD23 were generated from cynomolgus macaques immunized with
 purified soluble CD23 (sCD23). Four of the five primate antibodies blocked
 the binding of IgE complexes to CD23 positive cells and also inhibited the
 production of IgE in vitro by IL-4 induced human peripheral blood
 mononuclear cells (PBMC). The variable domains of several primate
 antibodies were utilized to construct chimeric macaque/human
 (PRIMATIZED((R))) monoclonal antibodies. PRIMATIZED((R)) p5E8G1,
 containing human gamma 1 constant region, inhibited IgE production in
 vitro as efficiently as the parent primate antibody, but the human gamma 4
 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE
 inhibition. An F(ab')₂ of p5E8G1 did not inhibit IgE production but did
 interfere with IgE inhibition by the intact anti-CD23
 antibody in a dose dependent fashion. The murine monoclonal
 antibody MHM6 recognizes human CD23 at a different epitope than primate
 antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with
 the F(ab')₂ of p5E8G1, the F(ab')₂ of MHM6 also failed to inhibit IgE
 production. These data imply that the mechanism by which anti-CD23
 antibodies inhibit IgE production requires cross-linking of CD23
 to an IgG receptor. These data also imply that neither bivalent
 cross-linking of CD23 alone or inhibition of CD23 binding to its natural
 ligands is sufficient to inhibit IgE production.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

purification, the report of frequent findings of I-CRM in normal and diseased liver may be accounted for by the present observation.

126 ANSWER 37 OF 37 MEDLINE DUPLICATE 17
80132519 Document Number: 80132519. PubMed ID: 6153592. The generation of memory B-cell subpopulations capable of proliferation and expansion of the pool; effect of time and antigen. Brooks K H; Feldbush T L; van der Hoven A. CELLULAR IMMUNOLOGY, 1990 Mar 15; 50:2:392-404. Journal code: 1046405. ISSN: 0008-8749. Pub. country: United States. Language: English.

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NEWS 4 Feb '1 TWILIT now produced by FIC Karlsruhe and has a new update frequency
NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective : 1. 2
NEWS 6 Mar '1 Gene Names now available in BIOSIS
NEWS 7 Mar 20 TWILIT no longer available
NEWS 8 Mar 20 FICUTHERMO no longer available
NEWS 9 Mar 28 US Provisional Priorities searched with P in CA CAPUS and USPATFULL
NEWS 10 Mar 28 LIPINSKI CALC added for property searching in REGISTRY
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 NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER
 NEWS 18 Apr 22 Federal Research in Progress FELRIP now available
 NEWS 19 Jun 03 New e-mail delivery for search results now available
 NEWS 20 Jun 19 MEDLINE Reload
 NEWS 21 Jun 15 FCIIFULL has been reloaded
 NEWS 22 Jul 02 FOREGE no longer contains STANDARDS file segment

NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
 CURRENT MACINTOSH VERSION IS V6.0a(ENG); AND V6.0Ja(JP),
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=> s ref: m3 au or k10etree: w3 au or nakamura t3 au
 L1 40543 REF: M3 AU OR FLOETTER W3 AU OR NAKAMURA T3 AU

=> s 11 and 6023 antibody
 L1 11 L1 AND 6023 ANTIBODY

=> dup remove 12
 PROCESSING COMPLETED FOR L2
 L3 3 DUF REMOVE L2 3 DUPLICATES REMOVED
 => d 13 1-3 chib abs

L3 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
 200204456 Document Number: 21957817. PubMed ID: 11962725. Anti-CD23
 monoclonal antibody inhibits germine Cepsilon transcription in B cells.
 Yabuuchi Shingo; Nakamura Takehiko; Kloetzer William S
 ; Reff Mitchell E. Seikagaku Corporation, Central Research
 Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp.
 Int Immunopharmacol, (2002 Mar) 2 (4): 453-61. Journal code: 100965259.
 ISSN: 1567-5769. Pub. country: Netherlands. Language: English.

AB A chimeric macaque/human (PRIMATIZED) anti-CD23 antibody
 , p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40
 antibody-stimulated IgE production by human peripheral blood mononuclear
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 Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data
 suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE
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L3 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
 2000150073 Document Number: 20150073. PubMed ID: 10684957. In vitro IgE
 inhibition in B cells by anti-CD23 monoclonal antibodies is functionally
 dependent on the immunoglobulin Fc domain. Nakamura T;
 Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J;
 Chinn P C; Morena R A; Shestowsky W S; Li Y F; Chen A; Reff M E.
 (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.)
 INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2): 131-41.
 Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United
 Kingdom. Language: English.

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 regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies
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 the binding of IgE complexes to CD23 positive cells and also inhibited the
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 mononuclear cells (PBMC). The variable domains of several primate
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 PRIMATIZED R monoclonal antibodies. PRIMATIZED R p5E6G1,
 containing human gamma 1 constant region, inhibited IgE production in
 vitro as efficiently as the parent primate antibody, but the human gamma 4
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 antibody in a dose dependent fashion. The murine monoclonal
 antibody MM6 recognizes human CD23 at a different epitope than primate
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 the Fab' 2 of p5E6G1, the Fab' 2 of MM6 also failed to inhibit IgE
 production. These data imply that the mechanism by which anti-CD23
 antibodies inhibit IgE production requires cross-linking of CD23
 to an IgE receptor. These data also imply that neither bivalent
 cross-linking of CD23 alone or inhibition of CD23 binding to its natural
 ligands is sufficient to inhibit IgE production.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

1999:779157 Document No. 192:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. **Reff, Mitchell R.**; Barnett, Richard Spence; McLachlan, Karen Petta **Idea Pharmaceuticals Corporation, USA).** U.S. US 5999144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors (Molly) and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, N1+Neomycin phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human **CD23 antibody** and immunoadhesin in Desmond marked CHO cells was achieved.

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
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DISCOUNT AMOUNTS FOR QUALIFYING ACCOUNTS	SINCE FILE	TOTAL
GA SUBSCRIBER PRICE	ENTRY	SESSION
	15.02	15.42

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frequency
NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6 Mar 08 Gene Names now available in BIOSIS
NEWS 7 Mar 22 TOXLIT no longer available
NEWS 8 Mar 22 TRCTHERMO no longer available
NEWS 9 Mar 28 US Provisional Priorities searched with P in CA/CAPLUS
and USPATFULL
NEWS 10 Mar 28 LIPINSKI/CALC added for property searching in REGISTRY
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NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 19 Jun 03 New e-mail delivery for search results now available
NEWS 20 Jun 10 MEDLINE Reload
NEWS 21 Jun 10 PCTFULL has been reloaded
NEWS 22 Jul 02 FOREGE no longer contains STANDARDS file segment
NEWS 23 Jul 19 NTIS to be reloaded July 28, 2002
NEWS 24 Jul 22 USAN to be reloaded July 28, 2002;
saved answer sets no longer valid

NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
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SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

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=> s chimeric CD23

L1 15 CHIMERIC CD23

=> s l1 and antibody

L2 6 L1 AND ANTIBODY

=> dup remove l2

PROCESSING COMPLETED FOR L2

L3 2 DUP REMOVE L2 (4 DUPLICATES REMOVED)

=> d l3 l-2 cbib abs

L3 ANSWER 1 OF 2 MEDLINE

2000384038 Document Number: 20304490. PubMed ID: 10845922. Engagement of CD11b and CD11c beta2 integrin by **antibodies** or soluble CD23 induces IL-1beta production on primary human monocytes through mitogen-activated protein kinase-dependent pathways. Rezzonico R; Chicheportiche R; Imbert V; Dayer J M. (Division of Immunology and Allergy, Clinical Immunology Unit (Hans Wilsdorf Laboratory), Department of Internal Medicine, University Hospital, Geneva, Switzerland.. rezzonico@unice.it). BLOOD. 2000 Jun 15; 95(12):3868-77. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English. beta2 integrins are involved in the recruitment of leukocytes to inflammatory sites and in cellular activation. We demonstrate that ligation of CD11b (Mac-1, CR3) or CD11c (p150, CR4) alpha chains of beta2 integrins by mAbs or soluble **chimeric CD23** (sCD23) on human freshly isolated monocytes rapidly stimulates high levels of interleukin-1beta production. This induction takes place at the transcriptional level and is regulated by members of the mitogen-activated protein kinase (MAPK) family. Indeed, stimulation of monocytes through engagement of CD11b or CD11c results in the phosphorylation and activation of ERK1, ERK2, and p38 MAPK MAP kinases. U0126, a potent inhibitor of the upstream activator of ERK1, 2, ie, MEK1, 2, suppresses IL-1beta messenger RNA mRNA expression in a dose-dependent fashion, showing the implication of this pathway in the transcriptional control of IL-1beta production. On the other hand, inhibition of p38 by SB203580 indicates that this MAPK is involved in the control of IL-1beta production at both transcriptional and translational levels. Together these data demonstrate that ligation of

repeated batch mode in a medium contg. 1 to 0.10 mM sodium butyrate.
Results showed that cells cultured in the presence of 0.03mM butyrate
showed a marked increase in antibody prodn. over the control.

=> s monoclonal
L5 727044 MONOCLONAL

=> s 15 and human CD23
4 FILES SEARCHED...
L6 42 15 AND HUMAN CD23

=> s 16 and chimeric
L7 7 16 AND CHIMERIC

=> dup remove 17
PROCESSING COMPLETED FOR L7
L8 3 DUP REMOVE L7 (4 DUPLICATES REMOVED)

=> d 18 1-3 cbib abs

L8 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:370546 Document No.: PREV200200370946. Antibodies against the stalk
region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis.
Caven, Timothy Hays (1; Ma, Check (1); Beavil, Rebecca; Beavil, Andrew;
Ghirlando, Rodolpho; Gould, Hannah; Conrad, Daniel (1. (1) Virginia
Commonwealth University, 1217 East Marshall Street, Richmond, VA, 23298
USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1239.
<http://www.fasebj.org/>. print. Meeting Info.: Annual Meeting of
Professional Research Scientists on Experimental Biology New Orleans,
Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language: English.
AB The stalk region of **human CD23** comprising a.a. 48-153
was expressed in *E. coli* and purified. In addition a **chimeric**
human CD23 was prepared consisting of the extracellular
region of CD23 linked to a modified leucine zipper (LZ-CD23). Polyclonal
antisera were produced in rabbits and shown to block binding of IgE to
CD23 both on cell surfaces as well as the interaction of LZ-CD23 with IgE
in an ELISA based assay. The antisera was also shown to inhibit IgE
synthesis in an anti-CD40/IL-4 stimulated human FBL model. The inhibition
was dose dependent and essentially complete blockage of IgE production was
seen at a relatively low dose of anti-stalk. FACS analysis using CD23+B
lymphoblastoid cells indicated little if any endocytosis and/or protection
from cleavage induced by the anti-stalk. **Monoclonal** antibodies
against the human stalk have also been prepared and these are being
analyzed for the capacity to inhibit IgE binding and IgE synthesis, as
well as compare their efficacy to the anti-lectin mabs. The results
indicate that targeting the stalk region is efficacious with respect to
blocking IgE production.

L8 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:186695 Document No.: PREV200200186695. Induction of apoptosis by IIEC-150
anti-CD23 in lymphoma cells. Fathan, Muzhat 1; Hariharan, Kandasamy
1; Hopkins, Michael; Saven, Alan; Refi, Mitchell 1; Hanna, Nabil 1;
Grint, Paul 1. IIEC Pharmaceuticals, San Diego, CA USA. Blood,
November 16, 2001 Vol. 98, No. 11 Part 1, pp. 367a.
<http://www.bloodjournal.org/>. print. Meeting Info.: 43rd Annual Meeting of
the American Society of Hematology, Part 1, Orlando, Florida, USA December
7-11, 2001 ISSN: 0006-4727. Language: English.
AB IIEC-150 is a primate-derived **monoclonal antibody to human**
CD23, the low-affinity receptor for IgE on B cells that has been
implicated in the regulation of IgE synthesis. In vitro and in vivo data
have demonstrated that IIEC-150 suppresses IgE synthesis. IIEC-150 is
currently in clinical trials for use in allergic asthma. CD23 is also

expressed at high levels in certain B-cell malignancies, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a **chimeric monoclonal antibody** to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the treatment of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain CD23 positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab)₂ fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of approx 10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong antibody dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of CD23, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

19 ANSWER 3 OF 3 MEDLINE
2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 **monoclonal antibodies** is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Klotzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2): 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcεvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five **monoclonal antibodies to human CD23** were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct **chimeric macaque/human (PRIMATIZED((R))) monoclonal antibodies**. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')₂ of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine **monoclonal antibody MHM6 recognizes human CD23** at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')₂ of p5E8G1, the F(ab')₂ of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-CD23 antibodies inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

=> 3 hits

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:25:09 ON
24 JUL 2002

L1 15 S CHIMERIC CD23
L2 6 S L1 AND ANTIBODY
L3 2 DUP REMOVE L2 4 DUPLICATES REMOVED
L4 1 S HUMANIZED ANTI CD23
L5 727044 S MONOCLONAL
L6 43 S L5 AND HUMAN CD23
L7 7 S L6 AND CHIMERIC
L8 3 DUP REMOVE L7 4 DUPLICATES REMOVED

=> s 15 and chimeric CD23
L9 1 L5 AND CHIMERIC CD23

=> d 19 cbib abs

L9 ANSWER 1 OF 1 MEDLINE

2000384038 Document Number: 20304490. PubMed ID: 10845922. Engagement of CD11b and CD11c beta2 integrin by antibodies or soluble CD23 induces IL-1beta production on primary human monocytes through mitogen-activated protein kinase-dependent pathways. Rezzonico R; Chicheportiche R; Imbert V; Dayer J M. (Division of Immunology and Allergy, Clinical Immunology Unit (Hans Wilsdorf Laboratory), Department of Internal Medicine, University Hospital, Geneva, Switzerland.. rezzonico@unice.it). BLOOD. (2000 Jun 15) 95 (12) 3868-77. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB beta2 integrins are involved in the recruitment of leukocytes to inflammatory sites and in cellular activation. We demonstrate that ligation of CD11b (Mac-1, CR3) or CD11c (p150, CR4) alpha chains of beta2 integrins by mAbs or soluble **chimeric CD23** (sCD23) on human freshly isolated monocytes rapidly stimulates high levels of interleukin-1beta production. This induction takes place at the transcriptional level and is regulated by members of the mitogen-activated protein kinase (MAPK) family. Indeed, stimulation of monocytes through engagement of CD11b or CD11c results in the phosphorylation and activation of ERK1, ERK2, and p38/SAPK2 MAP kinases. U0126, a potent inhibitor of the upstream activator of ERK1/2, ie, MEK1/2, suppresses IL-1beta messenger RNA (mRNA) expression in a dose-dependent fashion, showing the implication of this pathway in the transcriptional control of IL-1beta production. On the other hand, inhibition of p38 by SB203580 indicates that this MAPK is involved in the control of IL-1beta production at both transcriptional and translational levels. Together these data demonstrate that ligation of CD11b and CD11c beta2 integrins by mAbs or sCD23 fusion proteins triggers the activation of 2 distinct MAPK signaling pathways that cooperate in controlling IL-1beta synthesis at different levels. (Blood. 2000;95:3868-3877)

=> s 15 and humanized CD23
L10 0 L5 AND HUMANIZED CD23

=> d his

FILE 'HOME' ENTERED AT 08:04:54 ON 24 JUL 2002

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:05:09 ON
24 JUL 2002

L1 15 S CHIMERIC CD23
L2 6 S L1 AND ANTIBODY
L3 2 DUP REMOVE L2 4 DUPLICATES REMOVED
L4 1 S HUMANIZED ANTI CD23
L5 727044 S MONOCLONAL
L6 43 S L5 AND HUMAN CD23

L7 7 S L6 AND CHIMERIC
 L8 3 DUP REMOVE L7 4 DUPLICATES REMOVED
 L9 1 S L5 AND CHIMERIC CD23
 L10 0 S L5 AND HUMANIZED CD23

=> s l6 and IgE
 L11 38 L6 AND IGE

=> dup remove l11
 PROCESSING COMPLETED FOR L11
 L12 17 DUP REMOVE L11 21 DUPLICATES REMOVED

=> d l12 1-17 cbib abs

L12 ANSWER 1 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 2002:370946 Document No.: PREV200200370946. Antibodies against the stalk region of huCD23 block binding of **IgE** and inhibit in vitro **IgE** synthesis. Caven, Timothy Hays (1); Ma, Check (1); Beavil, Rebecca; Beavil, Andrew; Ghirlando, Rodolpho; Gould, Hannah; Conrad, Daniel (1). (1) Virginia Commonwealth University, 1217 East Marshall Street, Richmond, VA, 23298 USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1238. <http://www.fasebj.org/>. print. Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language: English.

AB The stalk region of **human CD23** comprising a.a. 48-153 was expressed in E. coli and purified. In addition a chimeric **human CD23** was prepared consisting of the extracellular region of CD23 linked to a modified leucine zipper (LZ-CD23). Polyclonal antisera were produced in rabbits and shown to block binding of **IgE** to CD23 both on cell surfaces as well as the interaction of LZ-CD23 with **IgE** in an ELISA based assay. The antisera was also shown to inhibit **IgE** synthesis in an anti-CD40/IL-4 stimulated human PBL model. The inhibition was dose dependent and essentially complete blockage of **IgE** production was seen at a relatively low dose of anti-stalk. FACS analysis using CD23-B lymphoblastoid cells indicated little if any endocytosis and/or protection from cleavage induced by the anti-stalk. **Monoclonal** antibodies against the human stalk have also been prepared and these are being analyzed for the capacity to inhibit **IgE** binding and **IgE** synthesis, as well as compare their efficacy to the anti-lectin mabs. The results indicate that targeting the stalk region is efficacious with respect to blocking **IgE** production.

L12 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2002 ACS
 2001:747174 Document No. 135:287537 Inhibitors for the formation of soluble **human CD23** and their use in treatment of diseases. Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142810 A1 20011010, 29 PP. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. English. CODEN: EPFXDW. APPLICATION: EP 2000-107515 20000407.

AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is described in which the overprodn. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. CD23 which inhibitor decreases or blocks selectively the activity of the metalloprotease ADAMP which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. CD23 is a **monoclonal** or polyclonal antibody directed against the metalloprotease ADAMP or wherein the inhibitor is an antisense oligonucleotide which is specific for ADAMP. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAMP as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders,

autoimmune diseases and allergy.

L12 ANSWER 3 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:196685 Document No.: PREV200200196685. Induction of apoptosis by IDEC-152 anti-CD23 in lymphoma cells. Pathan, Muzhat 1; Hariharan, Kandasamy 1; Hopkins, Michael; Saven, Alan; Reff, Mitchell 1; Hanna, Nabil 1; Grint, Paul 1. 1. IDEC Pharmaceuticals, San Diego, CA USA. Blood, November 16, 2001. Vol. 98, No. 11 Part 1, pp. 367a.
<http://www.bloodjournal.org/>. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971. Language: English.

AB IDEC-152 is a primatized **monoclonal** antibody to human **CD23**, the low-affinity receptor for **IgE** on B cells that has been implicated in the regulation of **IgE** synthesis. In vitro and in vivo data have demonstrated that IDEC-152 suppresses **IgE** synthesis. IDEC-152 is currently in clinical trials for use in allergic asthma. CD23 is also expressed at high levels in certain B-cell malignancies, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a chimeric **monoclonal** antibody to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the treatment of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain CD23 positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab)2 fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of approx10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong antibody dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of CD23, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

L12 ANSWER 4 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:320835 Document No.: PREV200000320835. Gamma-1 anti-human **CD23 monoclonal** antibodies. Reff, Mitchell E. (1); Kleetzer, William S.; Nakamura, Takehiko. 1. San Diego, CA USA. ASSIGNEE: IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6011138 January 04, 2000. Official Gazette of the United States Patent and Trademark Office Patents, Jan. 4, 2000. Vol. 1230, No. 1, pp. No pagination. e-file. ISSN: 0098-1133. Language: English.

AB Anti-human **CD23 monoclonal** antibodies containing human gamma 1 constant domains and therapeutic uses are provided. These antibodies inhibit IL-4 induced **IgE** production by B-cells significantly greater than antibodies containing other constant domains.

L12 ANSWER 5 OF 17 MEDLINE DUPLICATE 1
2001:151773 Document Number: 20151773. PubMed ID: 11674977. In vitro **IgE** inhibition in B cells by anti-**CD23 monoclonal** antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kleetzer W S; Bams F; Hariharan P; Chanat P; Jac A; LaBaire M C; Chinn P C; Morena F A; Szeszowski W F; Li Y F; Chen A; Reff M E. 1. Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.

INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 12(200 Feb), 22-32, 131-41.
Journal code: 7504759. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

- AB CD23, the low affinity receptor for IgE (FovarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED(R)) monoclonal antibodies. PRIMATIZED(R) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED(R) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-CD23 antibodies inhibit IgE production requires cross-linking of CD23 to an IgE receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

L12 ANSWER 6 OF 17 MEDLINE

2000150237 Document Number: 20150237. PubMed ID: 10684962.

Characterization of novel FcepsilonRII/CD23 isoforms lacking the transmembrane (TM) segment in human cell lines. Yoshikawa T; Matsui M; Gon Y; Yoshioka T; Hiram M; Lynch R G; Naito K; Yodoi J. (Institute for Virus Research, Kyoto University, 53 Kawahara-cho, Sakyo-ku, Kyoto, Japan.) MOLECULAR IMMUNOLOGY, (1999 Dec) 36 (18) 1223-33. Journal code: 7505289. ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.

- AB Human FcepsilonRII/CD23 is an approximately 45 kDa type II transmembrane glycoprotein belonging to the C-type animal-lectin family, and has two isoforms (a and b) that only differ in their intracytoplasmic tails. We previously found that in several human and mouse cell lines there were two additional CD23 transcripts (a' and b') lacking the exon 3 that encodes the entire transmembrane segment and a part of cytoplasmic tails. In this study, we analyzed the putative CD23a' and CD23b' products at protein levels and characterized with rabbit polyclonal antibodies against novel amino-acid sequences of the putative CD23a' and CD23b' molecules (anti-CD23a' Ab, anti-CD23b' Ab). Western blots in COS cells transfected with CD23a' or CD23b' cDNA as well as in vitro translation assays showed that the a' and b' CD23 transcripts were translated to about 40 kDa molecules. These 40 kDa molecules were also recognized by a polyclonal antibody against 25 kDa soluble fragment of human CD23. We also found that human cells having mRNAs for CD23a' and CD23b' expressed protein products recognized specifically by anti-CD23a' or anti-CD23b' Ab, respectively. In addition, the CD23a' and CD23b' molecules in transfected COS cells were resistant to Endo H f and PNGase F, although these truncated forms as well as the membrane-associated forms had an asparagine residue responsible for the N-linked glycosylation. Taken together, our results show that the a' and b' CD23 transcripts are expressed and translated in human lymphoid cells and that their translated products are retained in the cytoplasm where they might play an unique regulatory role in the expression of the full-length CD23 on the cell surface.

disclosed. The antibodies are useful for modulating or inhibiting induced **IgE** expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced **IgE** prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

- L12 ANSWER 10 OF 17 MEDLINE DUPLICATE 4
97351082 Document Number: 97351082. PubMed ID: 9207458. Inhibition of apoptosis in a human pre-B-cell line by CD23 is mediated via a novel receptor. White L J; Gnanne B W; Graber P; Aubry J F; Bonnefoy J Y; Cushley W. Institute of Biomedical & Life Sciences, University of Glasgow, Scotland, UK. BLOOD, (1997 Jul 15; 90 (1): 234-43. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.
- AB Human CD23 is a 45-kD type II membrane glycoprotein, which functions as a low-affinity receptor for **IgE** and as a ligand for the CD21 and CD11b/CD19 differentiation antigens. CD23 is released from the surface of cells as soluble fragments, and a 25-kD species of soluble CD23 (sCD23) appears to act as a multifunctional cytokine. In this report, sCD23 is shown to sustain the growth of low cell density cultures of a human pre-B-acute lymphocytic leukemia cell line, SMS-SB: no other cytokine tested was able to induce this effect. Flow cytometric analysis indicates that sCD23 acts to prevent apoptosis of SMS-SB cells. SMS-SB cells cultured at low cell density possess low levels of bcl-2 protein. Addition of sCD23 to cells at low cell density maintained bcl-2 expression at levels equivalent to those observed in SMS-SB cells cultured at higher cell densities. No CD23 mRNA was found in SMS-SB cells, ruling out an autocrine function for CD23 in this cell line model. Although SMS-SB cells do not express the known receptors for CD23, namely CD21, CD11b-CD19, or CD19-CD18, the cells specifically bind CD23-containing liposomes, but not glycophorin-containing liposomes. Binding of CD23-containing liposomes is inhibited by anti-CD23 but not by anti-CD21 or anti-CD11b/c **monoclonal** antibodies. The data show that sCD23 prevents apoptosis of the SMS-SB cell line by acting through a novel receptor.

- L12 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:463188 Document No.: PREV199699185544. Mechanism of T cell subsets and cytokines in the regulation of **IgE** production in exogenous asthma. Wang Danqi, Xia Guoguang (1); Zhao Shulin; et al. (1) Dep. Respiratory Med., Beijing Ji Shui Tan Hosp., Beijing 100035 China. Zhonghua Weishengwuxue He Mianyixue Zazhi, (1996) Vol. 16, No. 4, pp. 299-301. ISSN: 0254-5101. Language: Chinese. Summary Language: Chinese; English.
- AB The peripheral blood of 30 cases of asthma and 30 control adults were measured for T cell subsets with indirect immunofluorescence of **monoclonal** antibodies, for **IgE**, IL-4 with ELISA, for IL-3 with F123-cell line-biological method, for IL-6 with IL-6-dependent cell line TTD1 intake method and for CD3 with anti **human** CD23 McAb. The mechanism of T cells and cytokines in the regulation of **IgE** production in asthma and the effect of cytokines on the pathogenesis of asthma were also studied. The results showed that the levels of **IgE**, IL-4, IL-3, CD3, CD8+ as well as the ratio of CD4/CD8+ in cases of their acute stage were significantly different from those in their remission stage and normal controls $P < 0.01$. In their remission stage, there was no significant **IgE** difference between cases and control $P > 0.05$. And there were significant differences of CD8+ CD4/CD8 ratio between cases and normal controls $P < 0.01$. There was no significant difference of CD4, CD4, IL-6 among three groups $P > 0.05$. It indicated that the increased production of **IgE** antibody was the key factor in the pathogenesis of exogenous asthma and the cytokines played roles in the process of inflammatory reactions in the airway.

L12 ANSWER 12 OF 17 MEDLINE DUPLICATE 5
 9409240 Document Number: 9409240. PubMed ID: 7691616. CD21 expressed on basophilic cells is involved in histamine release triggered by CD23 and anti-CD21 antibodies. Bacon R.; Gauchat J F; Aubry J F; Poshon S; Graber P; Hentcho S; Bonnefoy J Y. Glaxo Institute for Molecular Biology, Plan-Les-Cuates, Geneva, Switzerland. EUROPEAN JOURNAL OF IMMUNOLOGY, 1993 Oct; 23 (10): 2721-4. Journal code: 1273261. ISSN: 0014-2980. Pub. country: GERMANY; Germany, Federal Republic of. Language: English.

AB Recombinant full-length human CD23 incorporated into fluorescent liposomes was used to detect a ligand for CD23 on the basophilic leukemia cell line, KU 812. Based on our recent finding that CD23 interacts with CD21 on subsets of B and T cells, we investigated if the same ligand was involved on KU 812 cells. An anti-CD21 monoclonal antibody (mAb) BU-33, was able to totally block CD23-liposome binding to KU 812 cells. Moreover, KU 812 cells express CD21 mRNA and have a cell surface molecule that reacts with anti-CD21 mAb. The CD23/CD21 interaction was not merely physical but was also associated with an increase in histamine release by KU 812 cells. Both recombinant soluble CD23 and an anti-CD21 mAb-mediated effect on histamine release was not restricted to and anti-CD21 mAb-mediated effect on histamine release was not restricted to the leukemic cell line, but was also observed with normal human blood basophils. These data demonstrate that CD21 is expressed on basophilic cells and that CD21 controls histamine production upon ligand-induced stimulation (CD23 or anti-CD21 mAb).

L12 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS
 1993:470048 Document No. 119:70048 The mechanisms of IgE uptake by human alveolar macrophages and a human B-lymphoblastoid cell line (Wil-2wt). Richardson, D. R.; Cameron, K.; Robinson, B.; Turner, K. J. (Dep. Microbiol., Univ. West. Australia, Nedlands, Australia). Immunology, 79(2), 305-11 (English) 1993. CODEN: IMMUM. ISSN: 0019-2805.

AB Human alveolar macrophages (HAM) internalized more IgE (81%) than human Wil-2wt B-lymphoblastoid cells (28%) suggesting a difference in the metabolic processing of the specific IgE receptor (CD23) or, alternatively, the presence of another functionally distinct receptor. The mannose receptor (MR), demonstrated to be present on the AM, may fulfill this role as IgE is heavily mannoseylated and binds to a greater extent to Con A (which has specificity for oligomannose oligosaccharide chains) than other antibody isotypes. The hypothesis of a second IgE receptor was tested using mannan which is a competitive inhibitor of ligand binding to the MR and mannoseylated bovine serum albumin (MBSA) which binds with avidity to the MR. Mannan (0.1 mg/mL) decreased internalized MBSA uptake in the HAM at 37.degree. suggesting the presence of the specific MR. In contrast, Wil-2wt cells did not bind MBSA. Mannan also reduced IgE uptake in the HAM at 37.degree. but had no effect on IgE uptake by Wil-2wt cells. Anti-CD23 monoclonal antibody mAb 135 also partially reduced membrane IgE uptake in HAM while completely inhibiting it by Wil-2wt cells. However, there did not appear to be competition for binding sites between IgE and MBSA in HAM. If only CD23 is involved in IgE uptake by HAM its function appears to be different to that in Wil-2wt cells. Definite involvement of the MR in IgE uptake will require further investigation as it may have an important role in allergic states.

L12 ANSWER 14 OF 17 MEDLINE DUPLICATE 6
 9314912 Document Number: 9314912. PubMed ID: 1385116. Cytokine effects of CD23 are mediated by an epitope distinct from the IgE binding site. Mossalayi M I; Azzam M; Delcresse G; Hotzstetter W; Bettler B; Talloul A H; Kishimoto E; Quast P; Lepre P; Sarfati M. Groupe d'Immun-Hematologie Molculaire, CHU Pitié-Salpêtrière, Paris, France. EMBO JOURNAL, 1992 Dec 15; 11 (24): 4103-9. Journal code: 0269664. ISSN:

- 0261-4189. Pub. country: ENGLAND: United Kingdom. Language: English.
- AB Human CD23 and its soluble forms sCD23 display various biological activities, in addition to their IgE binding function IgE/BF. The IgE binding domain was recently mapped to residues between Cys163 and Cys292 but its involvement in IgE-independent, CD23 functions remains unknown. In order to clarify this point, a series of N-terminal, C-terminal and internal deletion mutants of CD23 or sCD23 were expressed in CHO cells and tested for their ability i. to bind to IgE, ii. to induce colony formation by human myeloid precursor cells, iii. to promote mature T cell marker expression by early prothymocytes, and iv. to regulate IgE synthesis. The present study indicates that cytokine activities require the presence of Cys288, while this amino acid is not necessary for IgE/BF. Blocking experiments using various conformation-sensitive monoclonal antibodies further suggest that active epitope(s) of CD23 in cytokine assays is(are) distinct from those involved in IgE/BF.
- L12 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2002 ACS
1992:253891 Document No. 116:253891 Heterogeneity among Epstein-Barr virus-seropositive donors in the generation of immunoblastic B-cell lymphomas in SCID mice receiving human peripheral blood leukocyte grafts. Picchio, Gaston R.; Kobayashi, Ryo; Kirven, Marybeth; Baird, Stephen M.; Kipps, Thomas J.; Mosier, Donald E. (Div. Immunol., Med. Biol. Inst., La Jolla, CA, 92037, USA). Cancer Res., 52(9), 2468-77 (English) 1992. CODEN: CNREAS. ISSN: 0008-5472.
- AB Epstein-Barr virus (EBV) is assocd. with B-cell malignancy in immunosuppressed humans and SCID mice receiving human peripheral blood leukocyte grafts (hu-PBL-SCID). Here, the process of lymphoma development was further characterized in hu-PBL-SCID mice. EBV-seropos. donors differ markedly in the capacity of their PBL to give rise to immunoblastic lymphomas in SCID mice; some donors (high incidence) generated tumors rapidly in all hu-PBL-SCID mice, other donors (intermediate-low incidence) gave rise to sporadic tumors after a longer latent period (>10 wk), and some donors failed to produce tumors. B-cell lymphomas arising from high incidence donors were monoclonal in origin, and EBV replication was detected in all tumors. Tumors derived from intermediate-low incidence donors were monoclonal or oligoclonal and often had no evidence of viral replication. All tumors, regardless of the donor, resembled EBV-transformed lymphoblastoid cell lines in surface phenotype but differed from lymphoblastoid cell lines by having less Epstein-Barr nuclear antigen 2 and CD23 expression. The variable patterns of lymphomagenesis seen among different EBV-seropos. donors may be explained by lower levels of specific immunity to EBV in high incidence donors, permitting activation of EBV replication and potential transformation of secondary B-cell targets. In addn. there may be differences in the transforming potential of EBV infecting different donors. The use of the hu-PBL-SCID model may help predict patients at high risk for posttransplant or AIDS-assocd. lymphomas.
- L12 ANSWER 16 OF 17 MEDLINE DUPLICATE 7
*2364541 Document Number: 2364541. PubMed ID: 1386972. Demonstration of a second ligand for the low affinity receptor for immunoglobulin E (CD23) using recombinant CD23 reconstituted into fluorescent liposomes. Porchon F.; Glaber F.; Yeager M.; Jansen H.; Bernard A F.; Aubry J F.; Bonnefey J Y. Glaxo Institute for Molecular Biology, Plan-Les-Quates, Geneva, Switzerland. JOURNAL OF EXPERIMENTAL MEDICINE, 1992 Aug 1; 176: 399-407. Journal code: JEMEDR. ISSN: 0021-9127. Pub. country: United States. Language: English.
- AB Recombinant full-length human CD23 has been incorporated into fluorescent liposomes to demonstrate the existence of a ligand for CD23 that is different from the previously known ligand, immunoglobulin E (IgE). The novel ligand for CD23 is expressed

on subsets of normal T cells and B cells as well as on some myeloma cell lines. The interaction of full-length CD23 with its ligand is specifically inhibited by anti-CD23 monoclonal antibodies and by IgE, and it is Ca²⁺ dependent. Moreover, tunicamycin treatment of a CD23-binding cell line, RPMI 8226, significantly reduced the binding of CD23 incorporated into fluorescent liposomes, and a sugar, fucose-1-phosphate, was found to inhibit CD23-liposome binding to RPMI 8226 cells, suggesting the contribution of sugar structures on the CD23 ligand. In addition, CD23-transfected COS cells were shown to form specific conjugates with the cell line RPMI 8226. These data demonstrate that CD23 interacts with a ligand, which is different from IgE, and that CD23 can be considered as a new surface adhesion molecule involved in cell-cell interactions.

L12 ANSWER 17 OF 17 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 8
91341164 EMBASE Document No.: 1991341164. Expression of human recombinant CD23 in insect cells. Jansen K.U.; Shields J.; Gordon J.; Cairns J.; Graber P.; Bonnefoy J.-Y.. Glaxo Institute for Molecular Biology S.A. 46 route des Acacias, 1211 Geneva 24, Switzerland. Journal of Receptor Research 11/1-4 (507-520) 1991.
ISSN: 0197-5110. CODEN: JRERIM. Pub. Country: United States. Language: English. Summary Language: English.

AB Human CD23 (low affinity receptor for IgE) has been expressed in insect cells (Sf9) using the baculovirus expression system and the baculovirus transfer vector pAc373. Insect cells infected with a recombinant baculovirus coding for CD23 synthesized a polypeptide not found in wild-type infected insect cells that had antigenic properties similar to natural CD23 produced in RPMI 8866 cells. Surface expression of recombinant CD23 was demonstrated by its ability to bind IgE. Recombinant CD23 expressed in insect cells had a slightly lower molecular weight (43 kDa) than that of natural CD23 (45 kDa) from RPMI 8866 cells as detected by SDS-PAGE followed by Western-blotting. Affinity-purified recombinant CD23 from infected insect cells showed B-cell growth promoting activity. These observations demonstrate for the first time that biologically active recombinant CD23 can be produced by the baculovirus expression system, thus providing a useful source of recombinant material to elucidate the biological functions of CD23.

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:25:09 ON 24 JUL 2002

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11 15 S CHIMERIC CD23
12 6 S L1 AND ANTIBOD?
13 3 DUP REMOVE L2 4 DUPLICATES REMOVED
14 1 S HUMANIZED ANTI CD23
15 727044 S MONOCLONAL
16 43 S L5 AND HUMAN CD23
17 7 S L6 AND CHIMERIC
18 3 DUP REMOVE L7 4 DUPLICATES REMOVED
19 1 S L5 AND CHIMERIC CD23
20 5 S L5 AND HUMANIZED CD23
21 38 S L6 AND L5E
22 17 DUP REMOVE L11 21 DUPLICATES REMOVED

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=> s l11 and human gamma 1

1 FILES SEARCHED...

115 7 L11 AND HUMAN GAMMA 1

=> dup remove l15

PROCESSING COMPLETED FOR L12
L14 3 DUP REMOVE L13 4 DUPLICATES REMOVED

=> d 114 1-3 cbib abs

L14 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

0000:320835 Document No.: PREV200000320835. Gamma-1 anti-human
CD23 monoclonal antibodies. Reff, Mitchell E. 4 ;
Kloetzer, William S.; Nakamura, Takehiko. 1 San Diego, CA USA. ASSIGNEE:
IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku
Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6011138
January 04, 2000. Official Gazette of the United States Patent and
Trademark Office Patents, (Jan. 4, 2000) Vol. 1230, No. 1, pp. No
pagination. e-file. ISSN: 0098-1133. Language: English.

AB Anti-human **CD23 monoclonal** antibodies
containing human gamma 1 constant domains
and therapeutic uses are provided. These antibodies inhibit IL-4 induced
IgE production by B-cells significantly greater than antibodies
containing other constant domains.

L14 ANSWER 2 OF 3 MEDLINE DUPLICATE 1
2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro

IgE inhibition in B cells by anti-**CD23 monoclonal**
antibodies is functionally dependent on the immunoglobulin Fc domain.
Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M
J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E.
(Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.)
INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41.
Journal code: 7904799. ISSN: 0152-0561. Pub. country: ENGLAND: United
Kingdom. Language: English.

AB **CD23**, the low affinity receptor for **IgE** (Fc ϵ 2R), is
involved in regulation of **IgE** synthesis by B-lymphocytes. Five
monoclonal antibodies to human **CD23** were
generated from cynomolgus macaques immunized with purified soluble **CD23**
(sCD23). Four of the five primate antibodies blocked the binding of
IgE complexes to **CD23** positive cells and also inhibited the
production of **IgE** in vitro by IL-4 induced human peripheral
blood mononuclear cells (PBMC). The variable domains of several primate
antibodies were utilized to construct chimeric macaque/human
(PRIMATIZED((R))) **monoclonal** antibodies. PRIMATIZED((R)) p5E8G1,
containing human gamma 1 constant region,
inhibited **IgE** production in vitro as efficiently as the parent
primate antibody, but the human gamma 4 constant version, PRIMATIZED((R))
p5E8G4, was not as effective in **IgE** inhibition. An F(ab')₂ of
p5E8G1 did not inhibit **IgE** production but did interfere with
IgE inhibition by the intact anti-**CD23** antibody in a dose
dependent fashion. The murine **monoclonal** antibody MHM6
recognizes human **CD23** at a different epitope than
primate antibody 5E8, and inhibits **IgE** production by IL-4
induced PBMC. As with the F(ab')₂ of p5E8G1, the F(ab')₂ of MHM6 also
failed to inhibit **IgE** production. These data imply that the
mechanism by which anti-**CD23** antibodies inhibit **IgE** production
requires cross-linking of **CD23** to an **IgG** receptor. These data also imply
that neither bivalent cross-linking of **CD23** alone or inhibition of **CD23**
binding to its natural ligands is sufficient to inhibit **IgE**
production.

L14 ANSWER 3 OF 3 CASLUS COPYRIGHT 2002 ACS

1998:04984 Document No. 1998:04984 Gamma-1 and gamma-3 anti-human

CD23 monoclonal antibodies and use thereof as
therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko
Idec Pharmaceuticals Corp., USA; Seikagaku Corp., Jpn. Int. Appl. No.
98/00000 At 1998:04984, 147 pp. DESIGNATED STATES: W: AU, AM, AT, AR, AZ,

BA, BB, BG, BR, BY, CA, CH, CI, CJ, CK, CL, CM, CN, CO, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TP, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MP, NE, NL, PT, SE, SN, TD, TG. English.
 CODEN: PIXMD2. APPLICATION: WO 1998-052253 19980217. PRIORITY: US 1997-803085 19970220.

AB **Monoclonal antibodies** which specifically bind **human CD23**, the low affinity receptor for **IgE**. FcεRII/CD23, and contain either a **human gamma-1** or human gamma-3 const. domain, are disclosed. The antibodies are useful for modulating or inhibiting induced **IgE** expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced **IgE** prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

=> s IgE and allergy
 L15 9 IGE AND ALLERGY

=> s L15 and anti human CD23
 4 FILES SEARCHED...
 L16 0 L15 AND ANTI HUMAN CD23

=> s treatment
 L17 6822620 TREATMENT

=> s L17 and allergy
 L18 28761 L17 AND ALLERGY

=> s L18 and IgE
 L19 4493 L18 AND IGE

=> s L19 and antibody
 L20 2077 L19 AND ANTIBODY

=> s L20 and human CD23
 L21 2 L20 AND HUMAN CD23

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 L22 2 DUP REMOVE L21 (0 DUPLICATES REMOVED)

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L22 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
 0001:047174 Document No. 1351287537 Inhibitors for the formation of soluble **human CD23** and their use in **treatment** of diseases. Frey, Juergen Germany. Eur. Pat. Appl. EP 1140910 A1 2001010, 29 pp. DESIGNATED STATES: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. English.
 CODEN: EPXWVW. APPLICATION: EP 000140910 2001010.

AB A pharmaceutical compn. for the **treatment** or prophylaxis of disorders is described in which the overprodn. of **CD23** is implicated. This compn. comprises an inhibitor for the formation of human sol. **CD23** which inhibitor decreases or blocks selectively the activity of the metalloprotease **ADAM** which otherwise mediates the shedding of **CD23** in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. **CD23** is a monoclonal or polyclonal **antibody** directed against the metalloprotease **ADAM** or wherein the inhibitor is an antisense oligonucleotide which is specific

for c-myc. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and **allergy**.

L20 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. L29:215723 Gamma-1 and gamma-3 anti-human
CD23 monoclonal antibodies and use thereof as
therapeutics. Reff, Mitchell E.; Kioetzer, William S.; Nakamura, Takehiko
Idec Pharmaceuticals Corp., USA; Seikagaku Corp. PCT Int. Appl. WO
9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH,
GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, EE, FI, FR, GA,
GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English).
CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US
1997-803085 19970220.

AB **Monoclonal antibodies** which specifically bind human
CD23, the low affinity receptor for **IgE** (FcεRII/CD23),
and contain either a human gamma-1 or human gamma-3 const. domain, are
disclosed. **The antibodies** are useful for modulating or
inhibiting induced **IgE** expression. Accordingly, they have
practical utility in the **treatment** or prophylaxis of disease
conditions wherein inhibition of induced **IgE** prodn. is
therapeutically desirable, including allergic conditions, autoimmune
diseases and inflammatory diseases.

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L23 42663 (REFF M?/AU OR KLOETZER W?/AU OR NAKAMURA T?/AU)

=> s L23 and CD23 antibody
L24 11 L23 AND CD23 ANTIBODY

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L25 3 DUP REMOVE L24 (8 DUPLICATES REMOVED)

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L25 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
200224456 Document Number: 21957817. PubMed ID: 11962725. Anti-CD23
monoclonal antibody inhibits germline Cepsilon transcription in B cells.
Yabuuchi Shingo; Nakamura Takehiko; Kioetzer William S
; Reff Mitchell E. Seikagaku Corporation, Central Research
Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp.
Int Immunopharmacol., 2002 Mar 24 453-61. Journal code: 10965259.
ISSN: 1567-5769. Pub. country: Netherlands. Language: English.

AB A chimeric mouse/human **PRIMATIZED anti-CD23 antibody**
pGSG1, demonstrated a strong inhibitory effect on IL-4 and anti-CD43
antibody-stimulated IgE production by human peripheral blood mononuclear
cells PBMCs. RNA analysis by both reverse transcription-polymerase chain
reaction RT-PCR and Northern blot showed that pGSG1 inhibited germline
Cepsilon RNA synthesis, but had no effect on Cdelta mRNA levels. These data
suggest that pGSG1 may inhibit immunoglobulin class switching to IgE
through the inhibition of germline Cepsilon RNA synthesis. Early addition
of pGSG1 after stimulation by IL-4 and anti-CD43 was critical for IgE
inhibition. In contrast, later addition of pGSG1 still showed inhibition
of increased levels of surface CD23, which is normally upregulated by
stimulation with IL-4 and anti-CD43.

- L25 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
 2900159073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. **Nakamura T**; Kloezer W S; Brans P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena P A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan. INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 2000 Feb 22; 23: 131-41. Journal code: 7904789. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.
- AB CD23, the low affinity receptor for IgE Fc γ 2aR, is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) monoclonal antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')₂ of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')₂ of p5E8G1, the F(ab')₂ of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-CD23 antibodies inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.
- L25 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
 1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. **Reff, Mitchell R**; Barnett, Richard Spence; McLachlan, Karen Retta (Idex Pharmaceuticals Corporation, USA). U.S. 5 5998144 A. 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.
- AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenine deaminase, glutamine synthetase, and hypoxanthine-uridine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSC cells, B cell lines and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors, Molly, and vector combinations for use in the subret cloning method are also provided. This Molly vector contains dihydrofolatereductase, NI-Neomycin

phosphotransferase exon1, H2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and polsma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human **CD23 antibody** and immunoadhesin in Desmond marked CHO cells was achieved.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	113.11	113.32
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.58	-5.58

STN INTERNATIONAL LOGOFF AT 08:34:01 ON 24 JUL 2002